

AD _____

Award Number: DAMD17-01-1-0677

TITLE: Enabling Technologies for Advanced Soft Tissue Modeling

PRINCIPAL INVESTIGATOR: Steven L. Dawson, M.D.
Robert Howe, Ph.D.

CONTRACTING ORGANIZATION: Massachusetts General Hospital
Boston, Massachusetts 02114-2554

REPORT DATE: September 2002

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20030509 160

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)

2. REPORT DATE

September 2002

3. REPORT TYPE AND DATES COVERED

Annual (1 Sep 01 - 31 Aug 02)

4. TITLE AND SUBTITLE

Enabling Technologies for Advanced Soft Tissue Modeling

5. FUNDING NUMBERS

DAMD17-01-1-0677

6. AUTHOR(S)

Steven L. Dawson, M.D.

Robert Howe, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Massachusetts General Hospital
Boston, Massachusetts 02114-2554

E-Mail: dawson.steven@mgh.harvard.edu

8. PERFORMING ORGANIZATION
REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING
AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

Original contains color plates: All DTIC reproductions will be in black and white.

12a. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 Words)

Soft tissue properties represent a major and significant unknown in the domain of medical modeling and simulation. This program presents a 4 year research effort in defining tissue characteristics of three distinct organs - liver, spleen, and kidney- in vivo. Over the course of this program, we will use novel methods of tissue interrogation to characterize non-linear behavior during slow deformations, as would commonly be seen during surgical manipulations. We will then develop mathematical models which can be optimized to permit near real-time representations of organ behaviors, including the boundary characteristics of organs in situ. During this first year, we examined the in vivo deformations of porcine liver using two different instruments, and determined close agreement between the methods. We initiated mathematical models of our experimental measurements. We also established an experimental standard to compare different datasets, and to measure accuracy of mathematical models of tissue properties. These data were not previously known.

14. SUBJECT TERMS

tissue modeling, medical modeling and simulation, surgical training, mathematical modeling

15. NUMBER OF PAGES

39

16. PRICE CODE

17. SECURITY CLASSIFICATION
OF REPORT

Unclassified

18. SECURITY CLASSIFICATION
OF THIS PAGE

Unclassified

19. SECURITY CLASSIFICATION
OF ABSTRACT

Unclassified

20. LIMITATION OF ABSTRACT

Unlimited

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

Table of Contents

Cover.....	1
SF298	2
Introduction.....	4
Body.....	4
Design whole organ measurement tools	4
<i>Indentation-shear property tools</i>	4
<i>Implanted device</i>	5
Test tools and obtain measurements on ex-vivo tissue.....	6
<i>Indentation-shear property tools</i>	6
<i>Implanted device</i>	8
Validate measurements.....	8
<i>Indentation-shear property tools</i>	8
<i>Implanted device</i>	9
<i>Soft Tissue Reference Standard</i>	10
Initiate FEM models.....	10
Begin indentation testing of whole organs, end Year 1	10
Key Research Accomplishments	11
Reportable Outcomes.....	11
<i>Journal Papers</i>	11
<i>Conference Papers</i>	12
<i>Invited Lectures/Workshops/Meetings</i>	12
<i>Online resources</i>	12
Conclusions	12
"So What?"	13
Appendix A: Papers, Abstracts, Supporting Material.....	14
Appendix B: selected CVs and BioSketches	
Dawson, Steven L., M.D.	
Howe, Robert D., Ph.D.	
Ottensmeyer, Mark P., Ph.D.	
Kerdok, Amy E., M.S.	

Introduction

Computer-based medical modeling and simulation offers the potential for a completely new way to learn medical care. The use of computers as human assistants for medical diagnosis and training will require new knowledge domains. The most fundamental among these is the digital characterization of biophysical properties of perfused organs obtained from *in vivo* measurements, accounting for tissue properties integral to the organ as well as boundary conditions which affect the organ's global behavior.

Our research program is designed to obtain non-destructive measurements of living tissue—liver, spleen and kidney—from large animal models and to use this data to characterize non-linear behavior during large scale deformations, as would be seen in clinical practice. We are designing instruments to measure tissue properties and then creating mathematical models to allow representation of these data in a computer simulation. During the first year of research, we have studied small scale deformations of porcine liver *in vivo*, using both indentation and rotary shear measurements. We developed a useful standard reference object to examine general mathematical representations of deformation and published this standard at a publicly accessible website.

All work has been done according to institutional- and Defense Department-approved animal studies protocols.

Body

The following sections present our first year results organized according to the Statement of Work from our original research proposal. The points in that Statement include:

- Design whole organ measurement tools: indentation-shear property tool and implanted device
- Test tools and obtain measurements on *ex vivo* tissue
- Validate measurements using hand-held and motorized bench tools standards for *ex vivo* tissue
- Initiate FEM models
- Begin indentation testing of whole organs, end Year 1

Design whole organ measurement tools

Indentation-shear property tools

Our first device developed to measure the properties of tissue is the Tissue Material Property Measurement Tool (TeMPeST 1-D), which employs normal (perpendicular) indentation to apply forces to tissue and measure the force-displacement response [see Appendix A-Ottensmeyer, 2002a]. Since the ultimate goal of our research is the measurement of human tissues, this early instrument was designed for use in minimally invasive surgery. Successful completion of the instrument has demonstrated that building such an instrument is possible, and has highlighted numerous areas for improvement in future devices.

The TeMPeST 1-D (see Figure 1) is a 12mm diameter minimally invasive instrument, which can be used under laparoscopic conditions, or during open surgery. It can generate

arbitrary trajectories with a range of motion of $\pm 500\mu\text{m}$, forces up to 300mN, and bandwidth of approximately 80Hz.

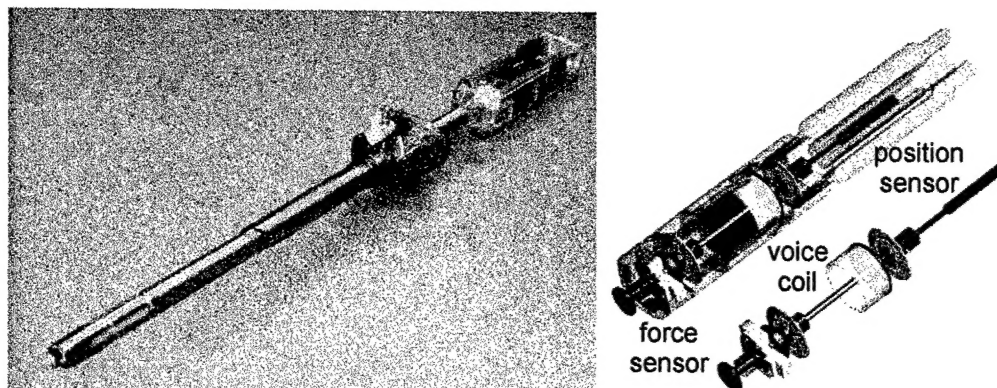


Figure 1: (left) TeMPeST 1-D instrument passing through standard 12mm surgical port. (right) Cutaway details of assembled sensor/actuator package and details of moving core elements

Through a collaboration with the Minimally Invasive Surgery Section of the University of Tübingen (Germany), we were also able to make use of the Rotary Shear Applicator (ROSA2), which applies a torsional shear load to tissues, while measuring the angular displacement of the contact head. The device, shown in Figure 2 (left and center), fixes the surface of the tissue with an outer ring (16mm inside diameter) while twisting the tissue with an inner contact head (6mm diameter). The issue of non-slip contact is critical for proper operation and measurement, so a variety of contact heads were investigated, including a densely packed needle array, a flat tip combined with surgical adhesive, and a novel surface modeled after the minute “teeth” of sharkskin.

The ROSA2 does not exhibit the same mechanical response as the TeMPeST 1-D, so a closed loop control system was developed for it, while still employing the same interface hardware and software as the TeMPeST 1-D.

Implanted device

The goal of the implantable device is to measure force, displacement, and velocity data on arbitrary local volumes within a whole organ to determine the complex material properties of the organ's native parenchymal tissue. A proof-of-concept device to accomplish this has evolved from the percutaneous retraction device described in the initial proposal. The idea behind the percutaneous retraction device was that a needle could be inserted into an organ and then a “T” would be deployed that would move within the organ as force, displacement, and velocity data are collected. However, this particular device is better suited for retracting hollow organs, and does not allow complete control of device configuration within the tissue.



Figure 2: (left) ROSA2 in contact with silicone gel test object (outer ring, optical position sensor visible); (center) ROSA2 with outer ring removed, showing flat tip; (right) detail of "rotary sharkskin" contact tip design¹

The T-needles are an initial prototype designed to completely control the device's orientation within the organ's tissue (collinear axis, constant initial separation between the parallel compression bars, perpendicular "T" configuration, etc.) such that a uniform strain field is applied to a local internal volume via parallel compression bars while force and displacement data are measured (Figure 3). FEM (finite element modeling) aided the design of the prototype by determining the necessary separation between the bars to neglect boundary condition effects (i.e. area under investigation is small compared to area of excised tissue) given a known *ex vivo* geometry of sample tissue. The needles are aligned using the v-block set-up and then two side needles containing the compression bars are inserted into the sample. The shafts are then inserted and screwed into the compression bars before the ends of the compression needles are removed (see Figure 4). The initial device is manually driven using a micrometer drive plate while force data is collected using a strain gauge.

Test tools and obtain measurements on ex-vivo tissue

Indentation-shear property tools

A variety of mechanical elements were used to validate the performance of the TeMPeST 1-D, including mechanical springs, masses, and three grades of silicone gel. Each of these materials was tested independently to determine their properties, so that the values measured by the TeMPeST 1-D would have a gold standard for comparison. The details of these tests are described in [see Appendix A-Ottensmeyer, 2002b], and demonstrate good agreement between TeMPeST 1-D measurements and the respective standards.

ROSA2 is an improved version of an earlier, larger device which was subject to excessive friction in the actuator. The initial work with ROSA2 involved determination of the calibration curve for the position sensor² and the torque constant for the galvanometer motor. Simultaneously, the system model for the instrument was determined so that a digital closed loop controller could be generated.

¹ This device has a diameter of 6mm, with feature sizes on the order of 0.1mm. One manufacturing technique (3-D printing, Z-Corp) has been determined to be unable to generate this geometry, and a search is ongoing for other suitable methods.

² An optical device which uses two polarized filters rotating with respect to each other. The nature of this system results in a non-linear (sinusoidal) relationship between angular position and sensor output voltage. Calibration and curve fitting permits extraction of angular data from the raw voltage.

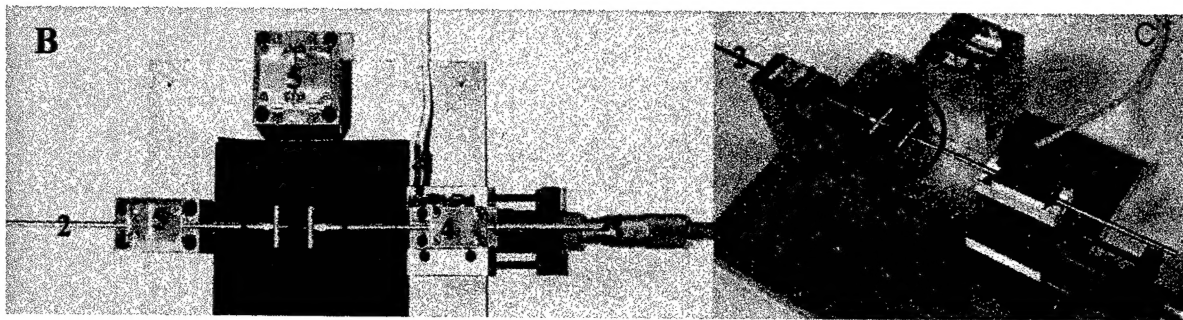
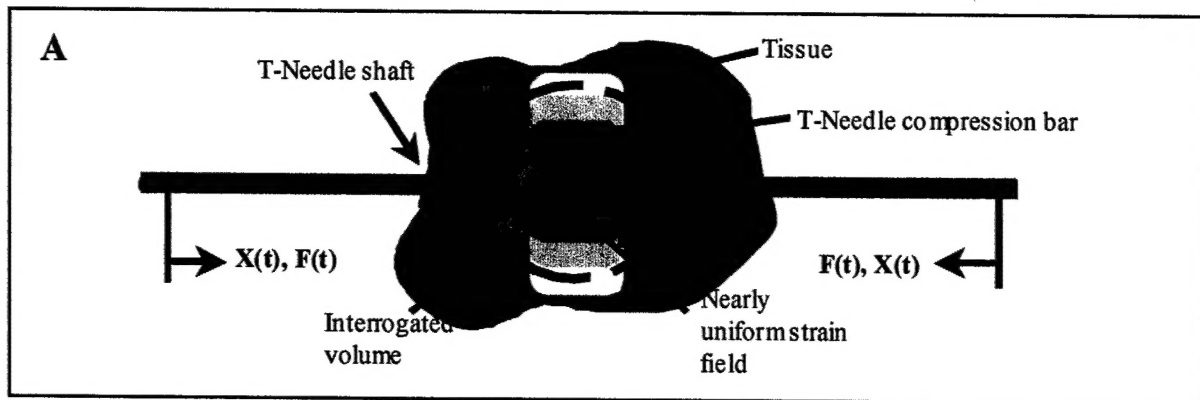


Figure 3: T-needle concept and initial prototype. (A) T-needle concept showing volume of parenchymal tissue under a nearly uniform strain field from displaced T-needle compression bars. The strain field produced goes from highest (red) in between the bars to lowest (yellow) outside the region of interest. Force, $F(t)$, and displacement, $x(t)$, as a function of time is applied and/or measured. (B) Top view and (C) angled view of T-needle prototype set-up. (1) 3mm diameter compression bars set 1.9 cm apart, (2) 3mm diameter shafts that move compression bars. (3) Micrometer drive plate. (4) Strain gauge one-axis force sensor. (5) V-block support and alignment system.

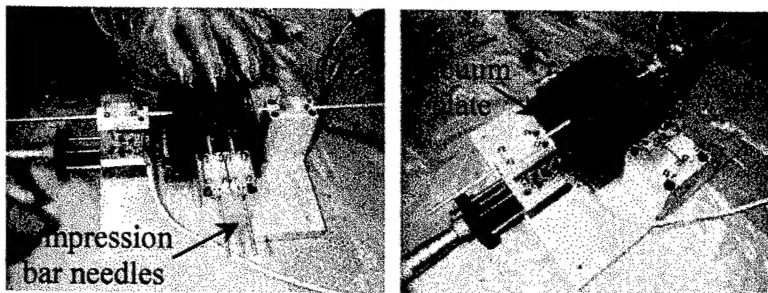


Figure 4: Freshly excised porcine liver test with T-needles. (left) Insertion of T-needles into vacuum mounted tissue sample. (right) Tissue sample ready for testing.

In parallel with testing of the instrument, contact heads were manufactured and tested for non-slip contact with various materials including silicone gels and *ex vivo* bovine liver samples. To facilitate this testing, the apparatus shown in Figure 5 was created. Rotation can be held fixed and the sample observed to determine at what angle slippage begins to occur. For both the tissue adhesive (Johnson and Johnson liquid bandage) and the needle array, angles without slip of up to 90° were achieved under static conditions.

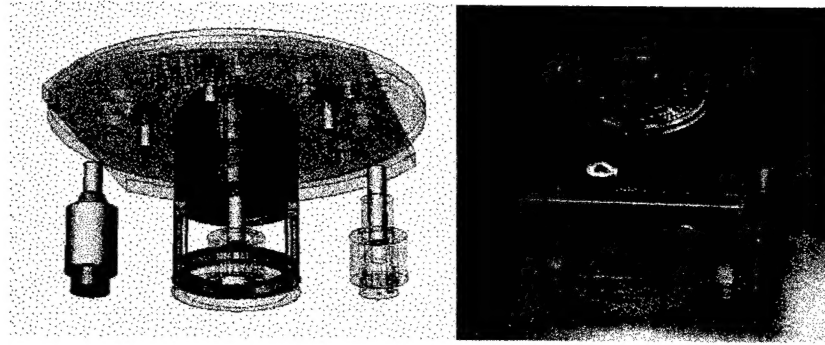


Figure 5: (left) static test rig with interchangeable contact heads; (right) test box with bovine liver sample.

Further testing was done on bovine liver samples to verify the qualitative results of finite element analysis (FEA) done at Tübingen with regards to rotation of tissue within the bulk of the organ. To achieve this, narrow gauge spinal needles were used to inject dilute barium sulfate solution into liver tissue and the static test rig was x-rayed with a medical fluoroscope as the contact head was rotated (see Figure 6). Numerical analysis of the images is ongoing, but initial results show agreement with the FEA.

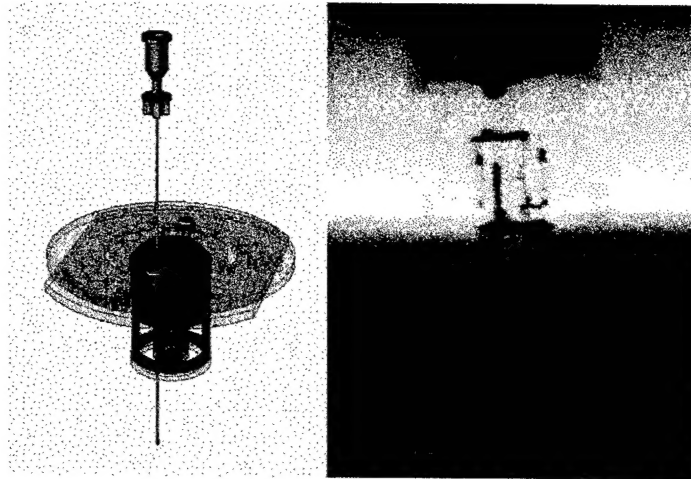


Figure 6: (left) static test rig with spinal needle for deposition of barium sulfate solution; (right) representative fluoroscope image showing injection paths and contact head.

Implanted device

The initial T-needle prototype was manipulated by hand and was tested on *ex vivo* samples of freshly excised and butcher bought porcine liver as well as silicone rubber (Figure 4). From these *ex vivo* results we were able to gain some insight on the behavior of soft tissue parenchyma (clearly a viscoelastic response). These initial experiments revealed changes that need to be made to obtain more accurate data. Such modifications and optimizations are discussed in the conclusions section.

Validate measurements

Indentation-shear property tools

The utility of the TeMPeST 1-D had been demonstrated prior to the start of this work, so the validation work emphasized the comparison between two testing paradigms (i.e. indentation vs. torsional shear) (see Figure 7).

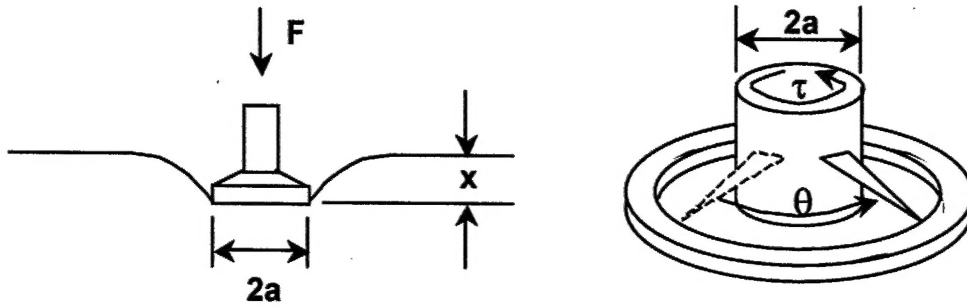


Figure 7: Two modes of tissue deformation: (left) normal indentation with applied force (F) and displacement (x) and (right) torsional shear with respect to fixed outer ring, showing applied torque (τ) and angular displacement (θ). Characteristic geometry defined by indenter radius, a .

Direct comparisons between the TeMPeST and ROSA2 were performed on silicone gel samples and on porcine liver *in vivo*. Analysis of the gel samples show that measurements of gel elasticity are the same to within better than a factor of two (see Figure 8). An early comparison of the same tests on bovine liver samples is also shown, which demonstrates identical frequency dependence in the compliance and phase data³.

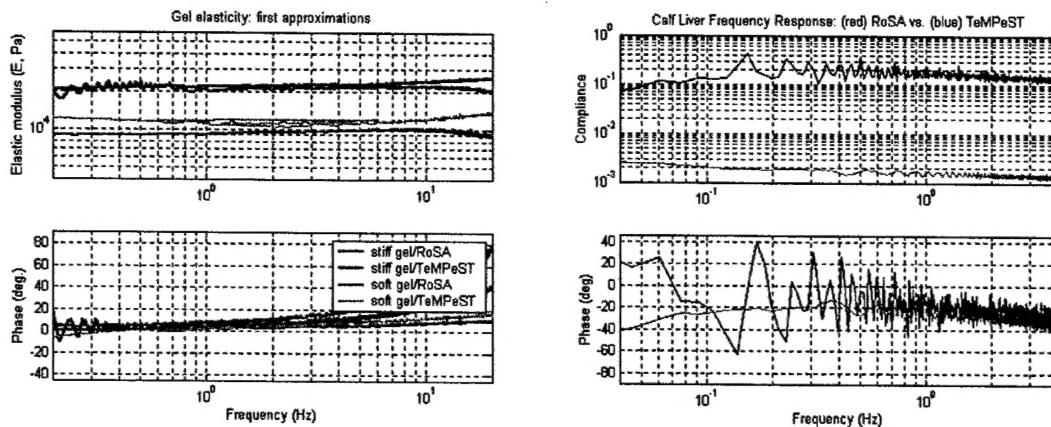


Figure 8: (left) silicone gel sample elasticity measurements; (right) bovine liver sample compliance measurements (units: m/N for TeMPeST, V_θ/V_i for ROSA2, where V_θ is position sensor output and V_i is the drive current control signal, both in Volts)

Implanted device

Each measurement made on the organ's components needs to be validated against some physical standard. With the material parameters and constitutive law defined and compiled for each component, the whole organ should also be validated against a physical standard. Lastly, due to the trade-offs made between fast computation time and accurate displacements in real-time computer simulations of soft tissue, there is a need for physical validation of these algorithms.

Testing the various components in multiple configurations and using inverse FE methods will serve as our means of validating each component of the organ.

³ The compliance curves are shifted due to the differences in output unit systems from the two instruments. Analysis to bring the data to a common format is ongoing.

Soft Tissue Reference Standard

As a first step toward a standard tissue atlas for particular solid organs, we designed an experiment to establish a benchmark for mathematical modeling of tissue deformations under non-linear displacements. This tissue phantom data has been posted on our website [<http://biorobotics.harvard.edu/truthcube/>] and can be used as a reference by other investigators who wish to test their models against a known dataset.

In Year 1, we designed and fabricated a geometrically regular solid test organ comprised of a well-defined material. This "Truth Cube" is an 8 x 8 x 8 cm silicone cube with discretely conspicuous internal fiducial markers which can be precisely tracked during computed tomographic (CT) imaging. The Cube was imaged in CT under known loading and boundary conditions (uniaxial compression and spherical indentation). The images obtained during loading conditions allowed us to measure internal displacements of the fiducials and create a Finite Element model of large scale deformations with known boundary conditions in the test object [see below, Appendix A-Kerdok & Howe, 2002].

Initiate FEM models

Finite Element Models (FEM) may be useful in medical simulation to represent complex systems such as whole organs. They are generally agreed to provide good representations of the mechanics of these complex systems. Such representations can be used in device design (see Section E.1.2) as well as material property prediction.

For comparison and validation purposes, we created FE models of the regular geometric solid organ phantom called the Truth Cube. [see Appendix A-Kerdock et al., 2002]. The FE models represented the three-dimensional system under uniform compression and spherical indentation. We were interested in determining what the simplest model could predict, and if more robust and elaborate FE models could predict the more complex loading conditions that would occur under larger strain and global deformations. In short, is finite element modeling an accurate method of representing medically important organ behaviors in surgical simulations?

We found that the finite element models can indeed predict the behavior of the material for small strains, but that the model breaks down for strains greater than 22%. Soft tissues have highly nonlinear material properties and are subjected to large deformations that exceed 30% strain during surgical manipulation. Therefore we concluded that although FE modeling is a useful and powerful tool for modeling small strain situations of many materials, it is merely an approximation method whose inherent limitations prevent it from being a viable whole-organ validation method. Physical measurements are currently much better suited for whole-organ validation. As part of our continuing research, we will investigate novel methods of mathematically modeling large scale deformations in our out-year program.

Begin indentation testing of whole organs, end Year 1

In vivo testing of TeMPeST 1D and ROSA 2 on the same organs in the same location has begun (see Figure 9) and will continue into the next year. Analysis will be performed as data becomes available. In addition to measurements of tissue compliance, additional evaluation of the non-slip behavior of the contact heads has been performed, as has histological analysis of the tissue underneath the contact heads. The former tests involved performing high-velocity step commands to the angular position of the ROSA2, and examining the torque-displacement response. In a number of cases with the needle array, evidence of slipping was observed (e.g.

changes in the mean angular position of the head, changes in angular position without corresponding changes in applied torque.) No slipping was observed when the tissue adhesive was used to ensure contact. Histological observations showed no damage occurred during testing. Angular displacements with the ROSA2 instrument are limited to $\pm 15^\circ$, which is significantly smaller than the range tested statically, so eventual testing in humans should similarly not result in tissue damage.



Figure 9: ROSA2 instrument being used to test porcine liver.

Key Research Accomplishments

- Established collaboration with U. Tübingen research group to acquire access to additional test instrument
- Validated comparability of torsional shear with normal indentation as a reliable method for measuring tissue properties
- Initiated parallel tests of ROSA2 and TeMPeST 1-D instruments on porcine liver *in vivo*
- Designed, developed, and initially tested a proof-of-concept prototype to internally deform a local volume of parenchymal tissue while recording force and displacement data
- Established a technique to create a physical standard of 3D whole-organ internal displacement fields
- Developed a web site and posted the initial raw data of the 3D internal strain fields of the silicone organ phantom (the Truth Cube)
- Showed that FE Models are an adequate validation tool for linearly elastic materials under low strains. A physical validation is needed for strains greater than approximately 25%.

Reportable Outcomes

Journal Papers

- Kerdok AE, Cotin SM, Ottensmeyer MP, Galea AM, Howe RD, Dawson SL: Truth cube: Establishing physical standards for real time soft tissue simulation. Medical Image Analysis (submitted for publication).

- Ottensmeyer MP: TeMPeST 1-D: an instrument for measuring solid organ soft tissue properties, *Experimental Techniques* 2002; 26, 48-50.

Conference Papers

- Ottensmeyer MP, Salisbury, Jr. JK,: In Vivo Data Acquisition Instrument For Solid Organ Mechanical Property Measurement, MICCAI 2001. Proceedings of the Medical Image Computing and Computer-Assisted Intervention 4th International Conference, Utrecht, The Netherlands, pp975-82. 14-17 Oct 2001.
- Ottensmeyer MP: In vivo measurement of solid organ mechanical tissue properties. Society for Experimental Mechanics Annual Meeting, Milwaukee, WI. pp328-333. 10-12 Jun 2002.
- Ottensmeyer MP: In vivo measurement of solid organ visco-elastic properties. MMVR02/10. Proceedings of Medicine Meets Virtual Reality 02/10, Newport Beach, CA. IOS Press. pp328-33. 23-26 Jan 2002.

Invited Lectures/Workshops/Meetings

- Ottensmeyer MP, Kalanovic D, Gross J: Comparison of indentation and rotary shear as modes for interrogating soft tissue visco-elasticity, SMIT2002, Proceedings of the 14th Annual Scientific Meeting, Oslo, Norway, 5-7 Sept 2002.
- Kerdok, AE, Howe, RD: Characterizing Soft Tissues for Surgical Simulation: Probing Parenchymal Properties, MIT Health Sciences and Technology 2002 Forum Abstract
- In vivo measurement techniques for determining mechanical responses of soft tissues. Tufts University Mechanical Engineering Seminar Series, 10 Apr 2002.
- Kerdok AE, Cotin SM, Ottensmeyer MP, Galea AM, Howe RD, Dawson SL: Truth cube: Establishing physical standards for real time soft tissue simulation, International Workshop on Deformable Modeling and Soft Tissue Simulation, Bonn, Germany, 14-15 Nov 2001.

Online resources

- Truth Cube website: <http://biorobotics.harvard.edu/truthcube/>

Conclusions

Analysis of the *in vivo* testing is ongoing, but qualitative results indicate the following: rotary shear does not cause damage to the tissue; rotary shear as a deformation mode is less sensitive than indentation to pulmonary action; maintaining contact with tissue using adhesive is more reliable than the use of a needle array (which may become clogged and slip); but application of the adhesive is an additional step that makes the measurement protocol more complex. Finally, a closed-loop control algorithm was developed to support use of the ROSA2 (which is not as amenable to open-loop control as the TeMPeST 1-D). This experience will be applied to the TeMPeST 1-D over the next year as in a number of cases, more precise control over the trajectory generated would be desirable. In addition, future generations of the TeMPeST instrument will incorporate design changes to make them less sensitive to pulmonary motions, most likely by grounding themselves against (and therefore moving with) the tissue rather than the operating table.

The T-needles are an initial proof-of-concept for measuring parenchymal properties of *ex vivo* tissue samples. However, it is obvious that the current design will not work well as our final "implantable" *in vivo* device. We are in the process of optimizing the T-needle's shape, size and performance. The initial studies revealed a need to reduce the stress concentrations and friction in the needles to ensure that we are uniformly compressing the tissue. We also noted the need to accurately measure the viscoelastic (time dependant) response of the tissue, and so the device is currently being equipped with a motor to enable the application of fast step displacements and loads while varying strain rate. Lastly, it was evident that *in vivo* or whole organs in a controlled environment would give much more repeatable and accurate results and a chamber is being built that will perfuse the organ, control the temperature, and minimize blood loss during testing.

Once we have accurate and reproducible data, we will work to redesign the system to incorporate multiple force-displacement modalities (shear, tension, compression, etc.) and to be more compatible to the constraints and conditions of an *in vivo* environment.

Our technique for recording the 3D internal strain fields of a solid volume has provided a physical standard for validation of whole-organ measurements. We will continue this work by applying the technique to whole organs and assessing other imaging possibilities.

FE Modeling will continue to aid in our device design. Once more organ data is collected an FE model of each test configuration will be developed for component validation and constitutive law determination.

"So What?"

The knowledge gained in the first year of this program establishes a path toward *in vivo* characterization of solid organ tissue behavior during clinically relevant manipulations. This information will be crucial to creation of effective medical training systems which can be designed to reproduce biological properties without requiring, for example, the use of animals for training. Although medical simulation holds much promise for changing the way medical knowledge has been imparted for millennia, truly effective learning of what to expect, how to react, and how to correct errors is the essence of medical wisdom. Without biological properties, computer graphics are just cartoons, devoid of relevance to patient care. But with biologically accurate behavior, computer simulations can become a replacement for learning on humans and animals. This work establishes one pathway to obtain the biological data to enable this transition.

Appendix A: Papers, Abstracts, Supporting Material

Ottensmeyer, 2002a

Ottensmeyer MP: TeMPeST 1-D: an instrument for measuring solid organ soft tissue properties, *Experimental Techniques* 2002; 26: 48-50.

Ottensmeyer, 2002b

Ottensmeyer MP: In vivo measurement of solid organ visco-elastic properties. MMVR02/10. *Proceedings of Medicine Meets Virtual Reality 02/10*, Newport Beach, CA. IOS Press. pp328-33. 23-26 Jan 2002.

Kerdok & Howe, 2002

Kerdok, AE, Howe, RD: Characterizing Soft Tissues for Surgical Simulation: Probing Parenchymal Properties, *MIT Health Sciences and Technology 2002 Forum Abstract*

Kerdock et al., 2002

Kerdok AE, Cotin SM, Ottensmeyer MP, Galea AM, Howe RD, Dawson SL: Truth cube: Establishing physical standards for real time soft tissue simulation, *International Workshop on Deformable Modeling and Soft Tissue Simulation*, Bonn, Germany, 14-15 Nov 2001.

TeMPeST I-D: AN INSTRUMENT FOR MEASURING SOLID ORGAN SOFT TISSUE PROPERTIES

Surgical simulation is a field that shows much promise in terms of permitting surgeons to learn new skills, as well as enabling the development of new procedures and instruments while minimizing the use of animal subjects. Essential to simulation with realistic force feedback are material property data for the wide variety of soft tissues, both in healthy and diseased conditions. Properties are known to change significantly after death, so measurements should ideally be made on living tissue. Further, tissue often has visco-elastic behaviors, so measuring properties over a range of frequencies is important. This paper presents the design of the TeMPeST 1-D (1-axis Tissue Material Property Sampling Tool) and its use in ongoing measurements of the visco-elastic properties of solid organ tissues.

As with engineering materials, the mechanical behavior of living tissue is governed by constitutive relationships that relate stress and strain (and often strain rate). Part of the problem of modeling tissue is choosing a suitable mathematical expression that captures observed behaviors like elasticity, stress relaxation and creep. Once a model is chosen, then the particular parameters that characterize the tissue need to be found. To do this, one needs to apply loads or displacements to tissue, measure the responses and then take geometry into account so that stress and strain (rate) are related instead of force and displacement.

DEFORMING TISSUES

Because of the wide variety of tissue and organ types, there are many different ways of determining tissue responses. Porcine brain was tested by Miller et al.¹ using a spherically tipped indenter executing a position ramp and hold under computer control. Carter et al.² have developed a hand-held indenter, which has been used on human liver during surgery. This instrument measures depth of indentation by comparing the position of the indenter with a surrounding ring that rests on the surface of the tissue. Tay et al.³ have made use of a small three degree of freedom (DOF) robot arm

equipped with a six DOF force-torque sensor and a right cylindrical tip to measure porcine esophagus tissues by indentation combined with shearing (transverse) motion. A number of groups have modified surgical instruments, equipping them with force and position sensors (Scilingo et al.⁴), as well as motors (Brown et al.⁵) to support computer control. With these instruments, the response of tissue to grasping can be measured. In the case of⁵, the grasper jaws are rectangular, simplifying the conversion from the force-displacement curve to material property. At least two groups have developed suction-based techniques in which a tube is sealed against tissue and the pressure lowered. The distance that the tissue bulges into the tube is measured optically. Aoki et al.⁶ use a clear tube, while Kauer et al.⁷ placed an angled mirror at the bottom of a tube with an offset hole cut in the end, which provides a profile view of the tissue surface to a camera placed at the top end of the tube. A rotary shear device that uses a circular probe with a dense array of needle tips to rotate the tissue while holding the surrounding tissue motionless with a larger ring (Kalanovic and Gross⁸) has been used on porcine liver.

TeMPeST I-D INSTRUMENT

The TeMPeST 1-D (Ottensmeyer⁹) (see Fig. 1) was designed explicitly to investigate the visco-elastic properties of tissue under small deformations. As testing of human tissues was a long term goal, a minimally invasive form was chosen so that it could be used either

during open or laparoscopic surgical settings. Portability was also an issue, so only the instrument and a laptop and docking station need to be brought into the operating theatre. The shaft of the instrument, which contains the force and position sensors and a voice coil actuator, can be separated from the handle so that the shaft can be sterilized. When in use, the instrument is rigidly fixed to the operating table with a laparoscope holder.

The instrument has a range of motion of $\pm 500 \mu\text{m}$, can exert forces up to 300 mN, and has an open loop mechanical bandwidth of approximately 80 Hz, which exceeds the bandwidth of human hand-eye and reflex control. The circular indenter tip has a diameter of 5 mm, and the overall diameter of the instrument is 12 mm, suitable for use with standard surgical cannulas (although 10 mm and 5 mm versions are more common). Figure 2 shows the detail of the sensor/actuator assembly, including the compression force sensor (modified Cooper Instruments & Systems (Warrenton, VA)

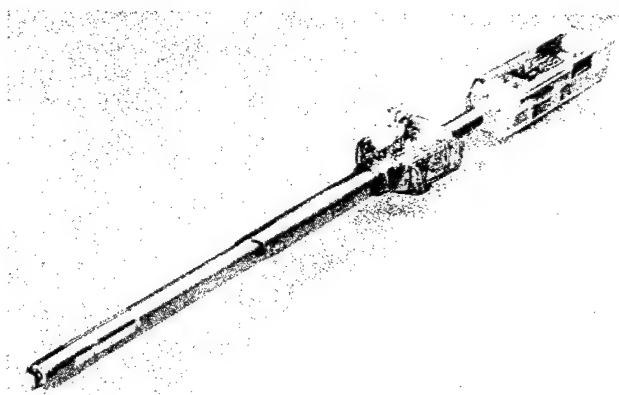


Fig. 1: TeMPeST I-D instrument inserted through 12 mm surgical cannula

Editor's Note: The new Biomechanics Feature Series will provide a forum for novel experimental techniques in the areas of biological and biologically inspired materials. This series will showcase development in advanced materials systems with an emphasis on biological, biomedical and biomimicry applications. Series Editor, K.E. Perry, Echobio.

M.P. Ottensmeyer is a Lead Investigator for Simulation Group, CIMIT, Cambridge, MA.

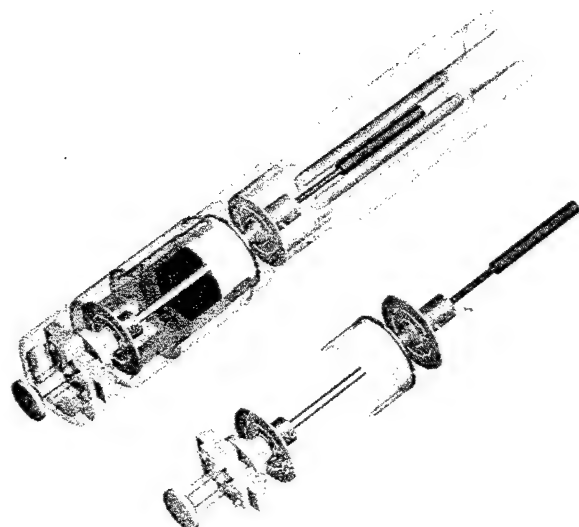


Fig. 2: Detail of sensor/actuator assembly. Flexural bearing-mounted moving core (right) consists of force sensor with circular tip, cylindrical voice coil and LVDT position sensor core. Cutaway view (left) shows magnet and pole-piece assembly.

LPM 562 500G), the custom made voice coil and rare earth magnet assembly, and the LVDT position sensor (Schaevitz (Hampton, VA) 099 XS-B).

Performance was verified on a variety of standard objects and materials including mechanical springs, standard masses and a number of silicone gels (GE RTV silicone gel 6166). Three different grades of the latter were created so that the results from a parallel plate rheometer could be compared with the TeMPeST 1-D results.

ANIMAL TISSUE TESTING

The instrument has been used to measure the responses of porcine liver and spleen *in vivo*, as well as rat liver, kidney, lung, heart and abdominal muscle *in vitro*.[†] For the *in vivo* testing, a typical animal tissue measurement sequence proceeds as follows. Ventilation with pure oxygen is suspended briefly so that breath motions are not measured superimposed on those generated by the instrument. A waveform, which may be sinusoidal, a chirp or some other arbitrary signal is commanded to the voice coil motor, which deforms the tissue with the 5mm punch. Sampling is complete in under 20 seconds, at which time ventilation resumes. A typical view through the laparoscope during testing is shown in Figure 3. Since the sampling interval is short and pure oxygen is used for ventilation, no harm comes to the animal during testing. Similarly, since the displacements of the tissue surface are small, no damage is incurred from the instrument. These issues are essential to consider early on, especially because successor instruments are planned for human use.

[†]All animal testing was approved by the relevant Institutional Animal Care and Use Committees.



Fig. 3: Laparoscopic view of indenter tip in contact with porcine liver

While the results of testing are frequency (and load) dependent stiffness values, they are dependent on the geometry of the indenter and the tissue being tested. For large, solid organs, a useful first approximation is that the tissue is isotropic and homogeneous (generally valid for liver or spleen), incompressible (approximately true for water-rich living tissue) and linear. This last assumption depends on the use of small deformations, relative to the size of the organ. Further, if the small deformation approximation is valid, then the organ can be treated as a semi-infinite body, which provides for closed form relationships between Young's modulus and the measured stiffness and the geometry of the indentation probe. In Equation (1) (adapted from Hayes et al.¹⁰), k is the measured stiffness, a , the radius of the indenter, K , a geometric factor which is unity for a semi-infinite body, and greater than one for a thin material on a rigid substrate, and finally E is Young's modulus (all in any consistent set of units).

$$E = K \frac{3k}{8a} \quad (1)$$

This expression can be extended to a frequency dependent form if k and E are replaced by functions of frequency, allowing viscous and inertial effects to be taken into account. An example of the results, showing E as a function of frequency and nominal stress (preload divided by indenter area) is shown in Figure 4.

For the case when the organ is small compared with the motion of the instrument (e.g. rat kidney), or when the tissue model is more complex than the extremely simplified one described, finite element models can be employed, iteratively approaching the observed response by modifying the parameters given the measured geometry and stiffness. Analysis of the rat kidney and liver data is ongoing.

SUMMARY

Measuring the material properties of living tissue is a complex problem, not only because of the nature of the tissues, but also because of the limits imposed by minimizing or preventing damage to the test subject. As a result a wide variety of techniques have been and continue to be developed, in-

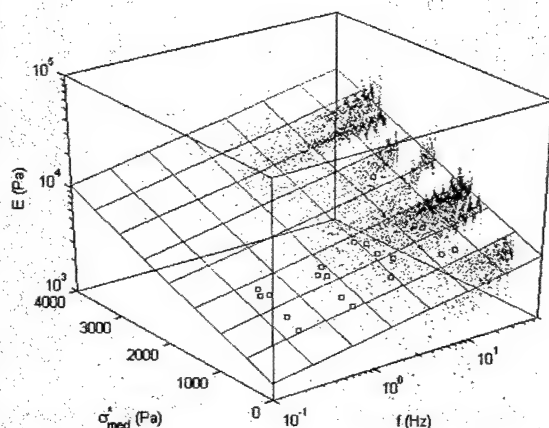


Fig. 4: Frequency dependent and non-linear elasticity of porcine liver. Squares are results from sinusoidal tests, point clouds from chirp response.

cluding non-invasive ones, employing external stimulation and imaging technology, as well as invasive techniques which directly contact and deform the tissue to be studied. No one technique is suitable to capture the full range of

behaviors, including non-linear stiffness, visco-elasticity, anisotropy and inhomogeneity. However each has its own advantages, and can be used to contribute data to and cross check the results of the others.

ACKNOWLEDGMENT

Portions of this work were supported by the Department of the Army, under contract number DAMD17-99-2-9001. The views and opinions expressed do not necessarily reflect the position or the policy of the government, and no official endorsement should be inferred.

References

1. Miller, K., Chinzei, K., Orssengo, G., Bednarz, P., "Mechanical Properties of Brain Tissue In-vivo: Experiment and Computer Simulation," *Journal of Biomechanics*, **33**, pp. 1369-76 (2000).
2. Carter, F.J., Frank, T.G., Davies, P.J., McLean, D., Cuschieri, A., "Measurements and Modeling of the Compliance of Human and Porcine Organs," *Medical Image Analysis*, **5**, pp. 231-236 (2001).
3. Tay, B.K., Stylopoulos, N., De, S., Rattner, D.W., Srinivasan, M.A., "Measurement of In-vivo Force Response of Intra-abdominal Soft Tissues for Surgical Simulation, Medicine Meets Virtual Reality 02/10," *Studies in Health Technology and Informatics*, **85**, pp. 514-519 (2002).
4. Scilingo, E.P., DeRossi, D., Bicchi, A., Iacconi, P., "Haptic Display for Replication of Rheological Behavior of Surgical Tissues: Modelling, Control, and Experiments," *Proceedings of the ASME Dynamics, Systems and Control Division*, pp. 173-176 (1997).
5. Brown, J.D., Rosen, J., Moreyra, M., Sinanan, M., Hannaford, B., "Computer-Controlled Motorized Endoscopic Grasper for In Vivo Measurements of Soft Tissue Biomechanical Characteristics, Medicine Meets Virtual Reality 02/10," *Studies in Health Technology and Informatics*, **85**, pp. 71-73 (2002).
6. Aoki, T., Ohashi, T., Matsumoto, T., Sato, M., "The Pipette Aspiration Applied to the Local Stiffness Measurement of Soft Tissues," *Annals of Biomedical Engineering*, **25**, pp. 581-587 (1997).
7. Kauer, M., Vuskovic, V., Dual, J., Szekely, G., Bajka, M., "Inverse Finite Element Characterization of Soft Tissues," *Proceedings of Medical Image Computing and Computer-Assisted Intervention, MICCAI 2001*, pp. 128-136 (2001).
8. Kalanovic, D., Gross, J., Center for Medical Research, Tuebingen, Germany, personal communication, 2002.
9. Ottensmeyer, Mark P., "In Vivo Measurement of Solid Organ Visco-elastic Properties, Medicine Meets Virtual Reality 02/10," *Studies in Health Technology and Informatics*, **85**, pp. 328-333 (2002).
10. Hayes, W.C., Keer, L.M., Herrmann, G., Mockros, L.F., "A Mathematical Analysis for Indentation Tests of Articular Cartilage," *Journal of Biomechanics*, **5**, pp. 541-551 (1972). ■

correlated SOLUTIONS

Turn the page in strain measurement technology ...



... to full field, non-contact strain analysis.

Produce surface strain plots for your entire test sample.
From complete, full scale aircraft wing assemblies
to microscale segments of biological tissue samples.

Consult the leaders in Digital Image Correlation.

www.CorrelatedSolutions.com

***In vivo* measurement of solid organ visco-elastic properties**

Mark P. Ottensmeyer, Ph.D.

Simulation Group, CIMIT, 65 Landsdowne St., rm 147, Cambridge, MA, 02139

mpo@alum.mit.edu

To support the ongoing development of software-based surgical simulation systems, work is underway to acquire the mechanical properties of living tissue. When such simulations include force feedback, visco-elastic properties must be evaluated over a range of frequencies relevant to human perception and motor control. A minimally invasive instrument has been developed which can perform normal indentation on solid organs, and apply and measure deformations over a frequency range from DC to approximately 100Hz. Measurement performance was validated on a series of objects and materials with known properties, and the device was subsequently used in *in vivo* tests on porcine liver. Results of these validation tests as well as the data extracted from the *in vivo* experiments are presented. Testing is ongoing, and will be expanded to more completely characterize liver, as well as porcine spleen and other solid organ tissues. While these animal tissue property tests are valuable in and of themselves, they pave the way for the development of instruments and experimental protocols suitable for the measurement of human tissue properties.

1. Introduction

One of the difficulties in developing realistic computer-based simulators for surgery is the scarcity of material properties for living tissue. Models which capture the mechanical behavior of tissues typically use estimates or *in vitro* measurements of the model parameters for given types of healthy or diseased tissues.

While estimates from experts may be suitable for surgical training, new instrument and new procedure prototyping will require more precise property values to closely match real organs. *In vitro* testing is useful as a place to begin, but because of changes like absence of blood perfusion and oxygenation, changes in boundary conditions, temperature, etc., one must also pursue *in vivo* acquisition to get accurate tissue property data.

Researchers are pursuing non-invasive [1, 2], minimally invasive [3, 4] and open surgical techniques [5, 6, 7]. Among the non-invasive techniques, are ultrasound [1] and MRI elastography [2], which make use of static or dynamic deformations at the surface of the body, and observations of the strain field imposed within the body. By performing

inverse calculations, elasticities of tissues relative to each other can be determined. This is, however, a complex process, and is highly dependent on knowledge of the relevant boundary conditions. The minimally invasive and open surgical techniques impose local deformations on tissue, and examine relatively local responses. [3] and [4] employ surgical instruments equipped with sensors to measure the local force-displacement response. [5], [6] and [7] use larger instruments to impose tensile loads, indentation or suction to tissues. By comparing the force-displacement responses with either simplified or finite element models of the tissue, again the inverse problem is solved to extract the tissue properties. These latter techniques can be computationally less expensive, and can impose larger deformations on tissue than the non-invasive techniques. However, they suffer limitations in that local measurements must be repeated at numerous locations over a given organ to yield a complete set of data. In addition, for organs with capsules (e.g. liver, spleen, or kidney), it may be difficult to differentiate the contributions to the measured stiffness of the parenchyma versus the capsule, since both structures are deformed simultaneously. For liver and spleen, which have relatively thinner/weaker capsules than kidney, this effect might be negligible, but further experiments will be necessary to find out what those contributions are.

In vivo tissue property measurement is still a young field, and the broad range of tissue types, the number of parameters needed to describe them, and the issues of age, type of disease and individual differences mean that there is still a need for additional data. No single technique will likely provide all of the data necessary, so all reliable data is a welcome contribution.

2. Methods and instruments

This research makes use of a single axis indentation device called the Tissue Material Property Sampling Tool (TeMPeST 1-D) [8, 9, 10]. It can pass through a 12mm surgical cannula or be used in open surgery, and generates small amplitude oscillations up to approximately 100Hz. Range of motion is $\pm 500\mu\text{m}$, and the maximum force that can be applied with a 5mm right circular punch is 300mN. Oscillations are generated by driving a voice-coil motor with a voltage controlled current amplifier.

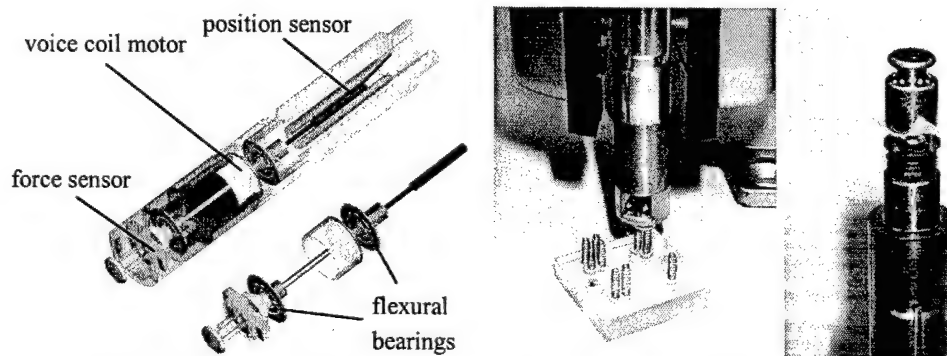


Figure 1. (left) Detail of sensor/actuator tip of TeMPeST 1-D and moving core elements. 12mm overall diameter. Force sensor is compression-only, suitable for indentation testing. Flexural bearings provide friction free support for voice-coil motor-driven core elements. Non-contact position sensing performed with LVDT sensor. (center & right) TeMPeST 1-D in validation tests on springs and inertial loads.

2.1. Validation Tests

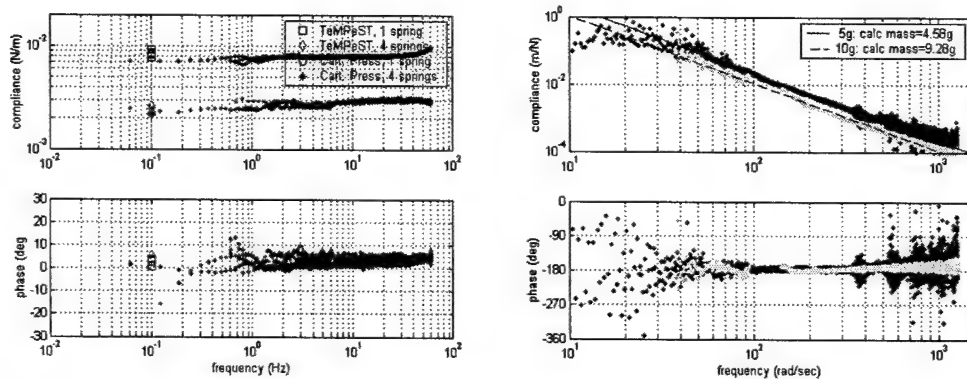


Figure 2. Frequency dependent compliance tests on springs and masses. For springs, TeMPeST 1-D frequency sweep data agree well with 0.1Hz fixed frequency (quasi-static) data, also with cartilage press instrument. For masses, fitting inertial load characteristic to data, yields good measurements of mass.

To verify that the instrument could be relied upon to provide accurate data, and to determine measurement limitations, a series of tests on mechanical springs (compliant loads), known masses (inertial loads) and silicone gels (visco-elastic materials) were performed. When tested over a range of frequencies, springs should exhibit a constant compliance, while for masses, the compliance should fall by two orders of magnitude while frequency increases by one order. As shown in Figure 2, both of these results are observed. Further, for the springs, the TeMPeST 1-D measurements agree with those made using a small compression testing device (cartilage press). Similarly, the masses calculated are close to the masses employed during testing.

Springs and masses have simple dynamic characteristics, so a series of silicone gels exhibiting visco-elastic responses within the bandwidth of the TeMPeST 1-D were created and tested. The gels were independently tested using a parallel plate rheometer, and again good agreement was obtained (see Figure 3).

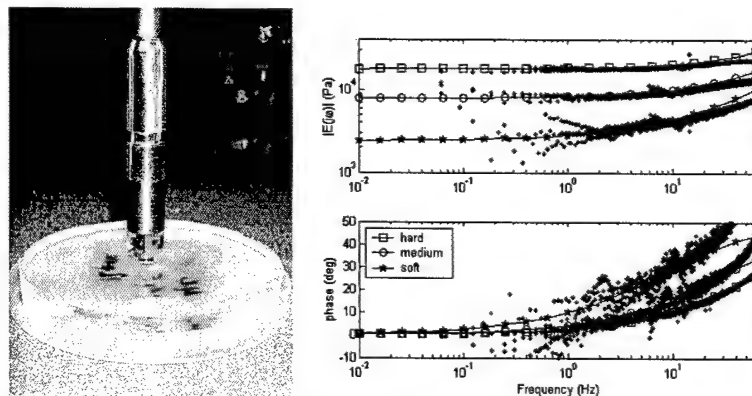


Figure 3. Visco-elastic material testing. Three different mixtures of two-part RTV silicone rubber were made and tested using a parallel plate rheometer (symbols) and compared with chirp data (point clouds) taken with the TeMPeST 1-D. For softest gel, force sensor signal to noise ratio is too small to obtain reliable data, providing lower limit of tissue stiffness that can be measured without modifications to the instrument.



Figure 4. TeMPeST 1-D instrument in use measuring porcine liver *in vivo*. TeMPeST 1-D visible in foreground (left), mounted on flexible laparoscope holder arm. Testing guided under laparoscopic camera guidance (handheld, background, and view shown at right).

The TeMPeST 1-D is being used in ongoing *in vivo* testing on porcine solid organs¹ to investigate viscous and non-linear elastic behaviors over the range relevant for haptics in surgical simulation. Figure 4 is an image from early, proof-of-concept testing, confirming that the instrument could be successfully employed in a minimally invasive environment. One disadvantage of this particular prototype, however, is that given the convex shape of most of the desirable internal organ surfaces, it is possible to make normal contact at at most one location on a given organ. To obtain data over the surface of the organ, one would require numerous insertion points, at least when used minimally invasively.

A series of tests was begun in conjunction with other researchers performing open surgical testing, which afforded access to large regions of the porcine liver. Anesthesia was achieved using an initial injection, and was maintained using an inhaled anesthetic throughout the testing. The pig was placed on pure oxygen ventilation, which could be suspended for periods of approximately 20 seconds. During this time, the TeMPeST 1-D was brought into contact with the surface of the organ with a predetermined pre-load force; the indentation waveform was generated with the voice-coil motor and imposed on the tissue for approximately 16.5 seconds; the TeMPeST 1-D was removed from the tissue and ventilation resumed. Blood oxygen saturation was monitored and was not observed to fall below 95% during testing.

3. Results

Tests on porcine liver have been performed using both sinusoidal and chirp signals, covering the frequency range of 0.01 to 100Hz, and preloads from 8 to 75mN. Within this range, the elastic modulus, calculated from the measured stiffness and the assumption of a semi-infinite, incompressible elastic medium, has been shown to be a non-linear function of mean applied stress (and therefore with strain) and frequency. A preliminary fit to the fixed frequency sinusoidal data takes the form:

$$\log_{10} E = 3.31 + 0.161 \log_{10} f + 2.15 E - 4\sigma_{med}^*$$

Equation 1

¹ All *in vivo* testing was performed under protocols approved by the animal use committees of all of the institutions involved. To minimize the number of animals used, testing was performed either as an addendum to a pre-existing protocol, or was performed together with other researchers conducting similar tests.

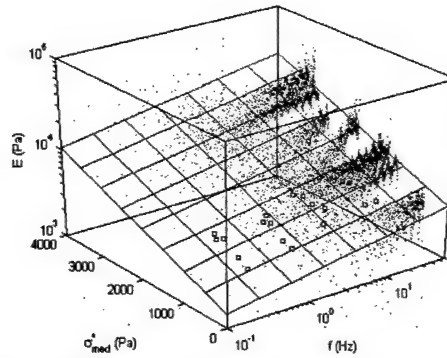


Figure 5. Chirp and fixed frequency sinusoidal data obtained *in vivo* from porcine liver.

where E is the elastic modulus in Pa, f is frequency in Hz, and σ_{med}^* is the median applied stress (median force/punch area). These data, and the fit are shown in Figure 5. What is clear from the testing performed to date is that the chirp tests, while convenient in terms of acquiring a range of frequency dependent data in one trial, have poor accuracy, so further testing will likely be performed using fixed frequency sinusoids.

Recognizing that the elastic modulus is the derivative of stress with respect to strain, this expression can be rewritten as:

$$\sigma = -2020 \ln(1 - 0.0005e^{7.62+0.161 \ln f \epsilon})$$

Equation 2

This fit is based only on the form exhibited by the data, rather than necessarily having a physical basis. As more data become available, parameters for more traditional models will be extracted.

4. Conclusions and ongoing work

The TeMPeST 1-D instrument for measuring visco-elastic properties of solid organ tissues has been completed. Validation testing on known materials was performed to verify the device's performance, and it has been used to gather frequency and stress dependent elasticity data for porcine liver.

Testing is ongoing, and tests planned for the remainder of 2001 and early 2002 include investigations of variation between individuals, inhomogeneity across organ surfaces, and tests of porcine spleen.

Based on the learning experience of these tests, the testing system will be further developed to be sensitive to a wider range of tissue stiffnesses; be less sensitive to disturbances caused by cardiac action; and eventually be modified for use on human organs. Ultimately, such properties will be used in creating surgical simulation systems, which would provide realistic force-feedback to end users from surgical students learning the basic skill required, to experienced surgeons refreshing their skills or developing new procedures.

Acknowledgements

This work was supported in part by the Department of the Army, under contract number DAMD17-99-2-9001. The views and opinions expressed do not necessarily reflect the position or the policy of the government, and no official endorsement should be inferred.

References

- [1] Maass, H., Kuhnappel, U.G.: Noninvasive measurement of elastic properties of living tissue, Computer Assisted Radiology and Surgery (CARS '99): proceedings of the 13th international congress and exhibition (1999) pp. 23–6.
- [2] Suga, M., Matsuda T., Okamoto, J., Takizawa, O., Oshiro, O., Minato, K., Tsutsumi, S., Nagata, I., Sakai, N., Takahashi, T.: Sensible Human Projects: Haptic Modeling and Surgical Simulation Based on Measurements of Practical Patients with MR Elastography—Measurement of Elastic Modulus, Medicine Meets Virtual Reality 2000, Studies in Health Technology and Informatics, 70, Newport Beach, CA (27–30 Jan 2000) pp. 334–40.
- [3] Rosen, J., Hannaford, B., MacFarlane, M.P., Sinanan, M.N.: Force Controlled and Teleoperated Endoscopic Grasper for Minimally Invasive Surgery—Experimental Performance Evaluation, IEEE Transactions on Biomedical Engineering, 46(10) (1999) pp. 1212–1221.
- [4] Scilingo, E.P., DeRossi, D., Bicchi, A., Iaconi, P.: Haptic display for replication of rheological behavior of surgical tissues: modelling, control, and experiments, Proceedings of the ASME Dynamics, Systems and Control Division, Dallas, TX (16–21 Nov 1997) pp. 173–176.
- [5] Brower, I., Ustin, J., Bentley, L., Sherman, A., Dhruv, N., Tendick, F.: Measuring In Vivo Animal Soft Tissue Properties for Haptic Modeling in Surgical Simulation, Medicine Meets Virtual Reality 2001, Studies in Health Technology and Informatics, 81, Newport Beach, CA (24–27 Jan 2001) pp. 69–74.
- [6] Miller, K., Chinzei, K., Orsengo, G., Bednarz, P.: Mechanical properties of brain tissue in-vivo: experiment and computer simulation. Journal of Biomechanics 33 (2000) pp. 1369–76.
- [7] Kauer, M., Vuskovic, V., Dual, J., Szekely, G., Bajka, M.: Inverse Finite Element Characterization of Soft Tissues, Proceedings of Medical Image Computing and Computer-Assisted Intervention, MICCAI 2001, Utrecht, Netherlands, (15–17 Oct 2001), pp. 128–136.
- [8] Ottensmeyer, M.P., Ben-Ur, E., Salisbury, J.K.: Input and Output for Surgical Simulation: Devices to Measure Tissue Properties in vivo and a Haptic Interface for Laparoscopy Simulators, Proceedings of Medicine Meets Virtual Reality 2000, Studies in Health Technology and Informatics, 70, Newport Beach, CA (27–30 Jan 2000) pp. 236–242.
- [9] Ottensmeyer, M.P., Salisbury, J.K.: In vivo mechanical tissue property measurement for improved simulations, Proceedings of Digitization of the Battlespace V and Battlefield Biomedical Technologies II, R. Suresh and H.H. Pien, Eds., Proc. SPIE 4037, Orlando, FL (24–28 Apr 2000) pp. 286–293.
- [10] Ottensmeyer, M.P., Salisbury, J.K.: In Vivo Data Acquisition Instrument For Solid Organ Mechanical Property Measurement, Proceedings of MICCAI 2001, Utrecht, Netherlands (15–17 Oct 2001) pp. 975–982.

Characterizing Soft Tissues for Surgical Simulation: Probing Parenchymal Properties

Amy Elizabeth Kerdok

Harvard University, HST-MEMP 1997

Robert D. Howe, Ph. D.

Division of Engineering and Applied Sciences, Harvard University

With the onset of minimally invasive surgery (MIS) surgeons are required to learn new skills for manipulating and visualizing 3D tissue from 2D images. Real time simulations of MIS are needed for training and planning. Developing realistic simulations is a formidable challenge. The overall project aim is to improve real time surgical simulation by developing mathematical models of soft tissues (liver, kidney, and spleen) under slow deformations typical of surgical manipulation, implementing new devices for measuring the necessary soft tissue material parameters for these models, and determining the natural boundary conditions of these organs. My focus is to develop tools needed to measure the material parameters of soft tissue parenchyma, model the observed behavior in the form of a constitutive law, and validate both the parenchyma and whole organ results.

The complex nature of soft tissue constituents (capsula, parenchyma, and vessels) needs to be addressed to make meaningful material property measurements. Tissue testing devices must account for tissue inhomogeneity, anisotropy, geometric and mechanical nonlinearity under large deformations, incompressibility, loading rate dependency, and viscoelasticity. A device has been developed to arbitrarily probe an internal, local volume of parenchyma under a uniform stress distribution *ex vivo*. The device applies known displacements while measuring forces between 2 cylindrical bars. Initial studies of the "T-Needle" prototype have been carried out on butcher bovine liver, silicone rubber, and freshly excised bovine liver. Results indicate a viscoelastic response. Modifications to the device are needed to produce repeatable results, and before *in vivo* studies can be performed.

A mathematical model will be developed to define the constitutive law of the parenchyma. Either a quasilinear viscoelastic type model with a strain energy function elastic response (i.e. Mooney Rivlin), or a biphasic model will be used initially to model the tissue's force-displacement response. Estimated material parameters, test loading conditions, and the measured displacements will serve as inputs to a finite element model that will output a predicted force to compare against the measured force. The chosen law will be optimized by testing it in several different loading conditions until the estimated material parameters converge.

The optimized model for each soft tissue constituent will be combined to model the organ of interest. A new technique is under development to validate this overall model. The goal is to provide accurate 3D internal strain field measurements that can be compared to the model's results under known boundary conditions. A "test organ" has been developed using a silicone rubber model with internal radiopaque markers whose positions are tracked under known loading conditions using CT. A similar approach will be used next on actual organs for overall validation.

This work is part of a project in conjunction with the CIMIT Simulation group at Massachusetts General Hospital, funded by the Army Medical Research and Materiel Command, and the Whitaker Foundation.

Truth Cube: Establishing Physical Standards for Real Time Soft Tissue Simulation

Amy E. Kerdok¹, Stephane M. Cotin², Mark P. Ottensmeyer², Anna Galea¹, Robert D. Howe¹, Steven L. Dawson²

¹ Division of Engineering and Applied Sciences, Harvard University

² CIMIT Simulation Group, Massachusetts General Hospital

kerdok@fas.harvard.edu, 29 Oxford St. Pierce Hall, Cambridge, MA 02138, USA
phone 617.496.9098, fax 617.495.9837, <http://biorobotics.harvard.edu>

Keywords: soft tissue modeling, medical simulation, real-time, finite element modeling, validation

Abstract

Accurate and real-time models of soft tissue behavior are key elements in the development of medical simulation systems. However, precise validation of these models remains a challenge. Currently, real-time modeling is at best validated against FEM models that have their own intrinsic limitations. This study is the first in a series that will develop physical standards resulting in a database of relevant information used to validate real-time soft tissue deformation. In this first study, a simple 8cm cube of silicone rubber with an exact pattern of embedded Teflon beads was tested in uniaxial compression while CT images were taken. The known material properties, geometry, and carefully controlled boundary conditions resulted in a complete set of volumetric displacement data. The results were also compared to an FEM analysis of an identical situation. This work has served as a proof of concept for a robust physical standard for use in validating real-time models. A web site has been created to provide access to our database at:

<http://biorobotics.harvard.edu/truthcube/>.

1. Introduction

Fast, realistic mechanical modeling of soft tissues remains a formidable challenge in the development of new medical applications. Medical training, surgical planning, and image-guidance systems require real-time calculation of tissue shape and interaction forces as the user manipulates the simulated tissue.

Implementation of these modeling systems has proved difficult. The most frequently used approaches to simulating tissue deformation in real-time have been spring-mass models and, more recently, finite element methods (FEM). This has proved relatively unsatisfactory: surgical applications involve large deformations of nonlinear soft materials and require very rapid calculations. Spring-mass systems have

limited accuracy but work in real-time, while FEM has proved successful for modeling small deformations of linear engineering materials where calculation speed is not a paramount concern. Many schemes have been proposed to overcome these limitations [e.g. Pic01, De01, Ast98, Kuh97, and Cot96], often balancing execution speed and mechanical accuracy. The nature of this tradeoff is not well understood, and it is difficult to evaluate the relative performance of new systems when speed, accuracy, tissue properties, and geometry all vary.

Progress towards effective real-time simulation would be aided by a consistent means of evaluating tissue mechanics models. Ideally, this evaluation method would provide a "gold standard" of experimental results for comparison with simulation results. This would take the form of fully specified material properties and stress, strain, and displacement fields throughout the tissue, under a range of fully specified and surgically relevant boundary conditions. The output of new modeling systems could then be compared to these standard results to validate and benchmark their performance.

We are working to create such a database of experimental measurements. The goal is to incorporate measurements for rubber phantoms with simple geometry and for a range of more complex materials including biological tissues and organs. These results will be archived on a web site for widespread access. This paper reports our initial effort, on the deformation of a cube of soft polymer. This 8 cm "truth cube" is made of a well-characterized silicone rubber with fiducials embedded in a 1 cm grid pattern throughout its volume. We have acquired computer tomography (CT) scans of the cube in undeformed and loaded states, and extracted the displacement of each fiducial using image processing techniques. Here we report these displacement results, along with details of the cube construction and boundary conditions in the loading tests. We conclude with a discussion of plans for extension of this work, and an invitation for

participation by others interested in the validation of fast large-deformation tissue modeling.

2. Methods

We have selected a cube as a simple, regular shape for this initial effort to assess the feasibility of the approach and develop the required techniques. The considerations include the materials of the "tissue" and fiducials, 3-D imaging, image processing, and data reporting.

2.1 Truth Cube

We selected a 2-part silicone rubber (RTV6166, General Electric Co.) because of its proven success in simulating tissues [Ott00, Wel99]. The material is soft but exhibits linear behavior to at least 30% strain. To enable tracking of the internal displacements of the cube we embedded small beads as fiducials that would readily appear in CT scans but not significantly alter the material properties of the silicone. The choice of bead material and size was motivated both by the need for high contrast without creating imaging artifacts [Str98]; this implies a specific gravity well above silicone (0.98) but much less than steel (~ 8). To enable accurate segmentation and position estimation, the minimum diameter of the beads had to be slightly larger than the distance between two successive scanning planes (1.25 mm) but small enough to avoid compromising the material properties of the silicone. Imaging tests revealed that Teflon beads (specific gravity 2.3) with a diameter of 1.58 mm fulfilled all of these criteria.

The mold for the cube had removable sides, with the bottom serving as a rigid permanent mounting plate and was roughened and dimpled to ensure complete adhesion of the silicone. The two-part silicone rubber was mixed in a 30:70 proportion to obtain material characteristics similar to that of soft tissue. A layer 1 cm deep was poured, the mold was placed in a vacuum chamber to remove air bubbles, and then allowed to set on a leveled surface (~ 3.5 hours) before positioning the beads in a 7×7 matrix spaced 1 cm apart (Figure 1). The beads were laid on the rubber using a matrix of bead positioning tubes and allowed to set into the rubber for at least another hour before the next layer was poured. The end result produced an 8 cm^3 silicone rubber cube with 7 rows and 7 columns of Teflon® beads in 7 layers spaced 1 cm apart (Figure 2).

To ensure that the material properties of the silicone rubber were not affected by the addition of the 343 beads, we performed indentation tests on a sample of

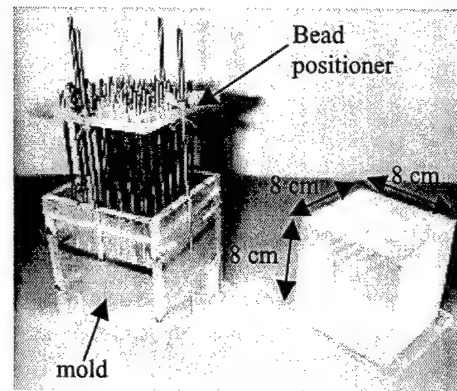


Figure 1: (left) Mold and bead positioner and (right) resulting "Truth Cube"

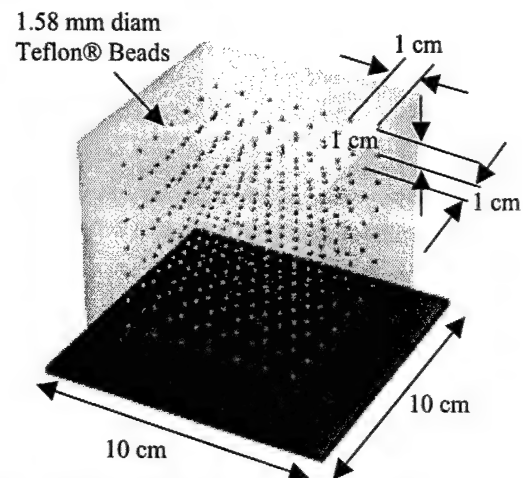


Figure 2: Dimensional drawing of "Truth Cube"

the silicone rubber alone, on a sample with sparse bead density, and on a sample with 1 cm bead spacing. Results indicated that the stiffness of the sample with the highest bead density (780 N/m) changed 2%, less than the 4.4% standard deviation of measurements of the plain sample. We thus assume that the addition of the beads had a negligible effect on the material properties of the silicone.

A small strain ($<4\%$) uniaxial compression test was performed on the final cube to obtain material property characteristics. Results indicate a Young's modulus of 25.8 kPa. We assume that Poisson's ratio is near 0.5 for this polymer; volumetric data from the loaded state below showed minor compression, but this difference was less than the measurement accuracy.

2.2 Experimental Set-up

The test set-up for loading the cube must apply carefully controlled boundary conditions during the CT imaging process. The fixture base was constructed of 25.4 mm thick PVC (specific gravity 1.37) to span the width of the scan table for support (Figure 3). A pocket that tightly fit the rubber cube's base plate was cut into the fixture base. To ensure accurate positioning of the cube each time it was tested, various reference features were incorporated into the test fixture. The fixture base also included registration markers consisting of machined holes and grooves in "X" patterns, and Delrin spheres (specific gravity 1.4) positioned at the cube base corners and on top of a central post (visible in Figure 4A, B).

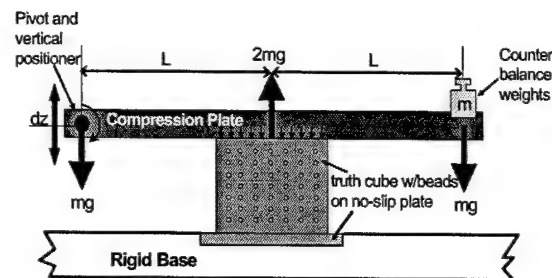


Figure 3: Side view of the experimental set-up. L is the length from the loading points to the center of the cube, dz is the vertical motion, and m is the mass of the counter weights.

The initial loading test reported here, uniaxial compression, was accomplished with a 25.4 mm thick acrylic plate (specific gravity 1.17). This was attached by a low-friction pivot to a vertical support. The plate was loaded by metal weights applied to the end opposite the pivot (in addition to the weight of the plate itself). The design confined all metal parts (the vertical support rods and weights) to the ends of the apparatus, so that they did not interfere with CT scanning of the cube in the middle of the apparatus. A linear dial indicator measured the distance the plate was compressed.

2.3 Experimental Protocol

A first scan of the experimental setup was performed while the cube was unloaded. The flat compression plate was then held level as it was lowered onto the oiled top surface of the cube to a set displacement. With the pivot end of the compression plate held in place, masses were added to a pocket in the other end until equilibrium was established as determined by level indicators. Three loading conditions were scanned: 4 mm, 10 mm, and 14.6 mm displacements

producing 5.0%, 12.5%, and 18.25% nominal strain respectively.

Once loaded, the cube was scanned in a General Electric LightSpeed CT scanner. Volumetric images of the "truth cube" were then obtained using the following scanner settings: 120kV, 180mA, standard reconstruction type, and high quality scan mode. The field of view was of 190 mm, producing a voxel size of $0.37109 \times 0.37109 \times 1.25 \text{ mm}^3$. Each CT scan was composed of 99 slices (512×512 pixels, 16 bits) exported in DICOM format.

2.4 Image Processing

Commercial software (3D-Doctor, Able Software Corp., Lexington, MA) was used for manipulating the volumetric images. First, the minor artifacts present in the lower part of the cube (due to the PVC support plate) were filtered. Second, fiducial beads in each of the scans were segmented from the gel with thresholding; this was straightforward due to the relatively good contrast between the beads and the silicone gel, and all 343 beads were readily extracted. Surface models were then calculated in a format suitable for further processing.

The beads in the silicone cube have a size close to the size of a voxel, so the three-dimensional segmentation process only provided an approximation of the shape and location of the beads. To further analyze the data it was necessary to accurately determine the location of the center of each bead. We implemented a least squares algorithm that fit a sphere to the set of points defined by the vertices of the segmented beads. This algorithm is part of visualization software that visually assesses the quality of the fit, saves the information to files, and displays polygonal models and vector fields.

Computation of the displacement vectors of the beads between various loading conditions required the solution of a relatively complex matching problem. We therefore used a manual matching approach for this first set of experiments. Finally, the outermost three-dimensional surfaces of the cube at each compression stage were extracted from the images. Registration marks were also segmented in order to evaluate potential motion of the experimental setup between successive scans.

2.5 Finite Element Model Comparison

A finite element model of the truth cube using commercial FEM software (ABAQUS v. 5.8, Hibbitt, Karlsson & Sorensen, Inc., Pawtucket, Rhode Island) was computed to compare with the experimental

results. A mesh was manually generated consisting of 10 mm, 8-node, solid cube linear elements. The cube's material properties (as measured in [Ott01]) are isotropic and linear with a Young's modulus of 15.3 kPa and an assumed Poisson's ratio of 0.499. Large deformation (i.e. nonlinear) analysis was employed using the boundary conditions and geometry extracted from the CT scans for the unloaded and 18.25% nominal strain cases.

3. Results

Figure 4 illustrates the processing of the data, beginning with segmented CT data for the x - z slice through the center of the cube, in both unloaded (Figure 4A) and 18.25% strain (Figure 4B) cases. Figure 4C shows the bead displacements throughout the cube combined for all four strain levels, while Figure 4D represents the displacement field for the central x - z slice. Reconstructions of the outer surface of the cube for each strain state is shown in Figure 4E. The estimated error of the bead locations is 2 mm.

The results from the FEM model are shown in Figure 5A, in the form of a plot for the x - z slice through

the center of the cube with displacement magnitude coded as color. Figure 5B shows the FEM and experimental displacement vectors for each bead in this slice. The coordinates of a sample of 10 of the beads are presented in Table 1, together with their displacements from the FEM and experimental measurements, and the differences between these estimates. Full results are available on the project web site, <http://biorobotics.harvard.edu/truthcube/>.

4. Discussion

The results presented here demonstrate the potential of this technique for establishing physical standards for validating real time soft tissue simulations. The construction of the cube was straightforward and resulted in a structure with a modulus in the range of soft organs. Imaging under strains of over 18% was readily accomplished. The external surface and the fiducial beads were easily segmented, which permitted calculation of the displacement fields throughout the volume. The result is a displacement data set with well-characterized material properties and boundary conditions.

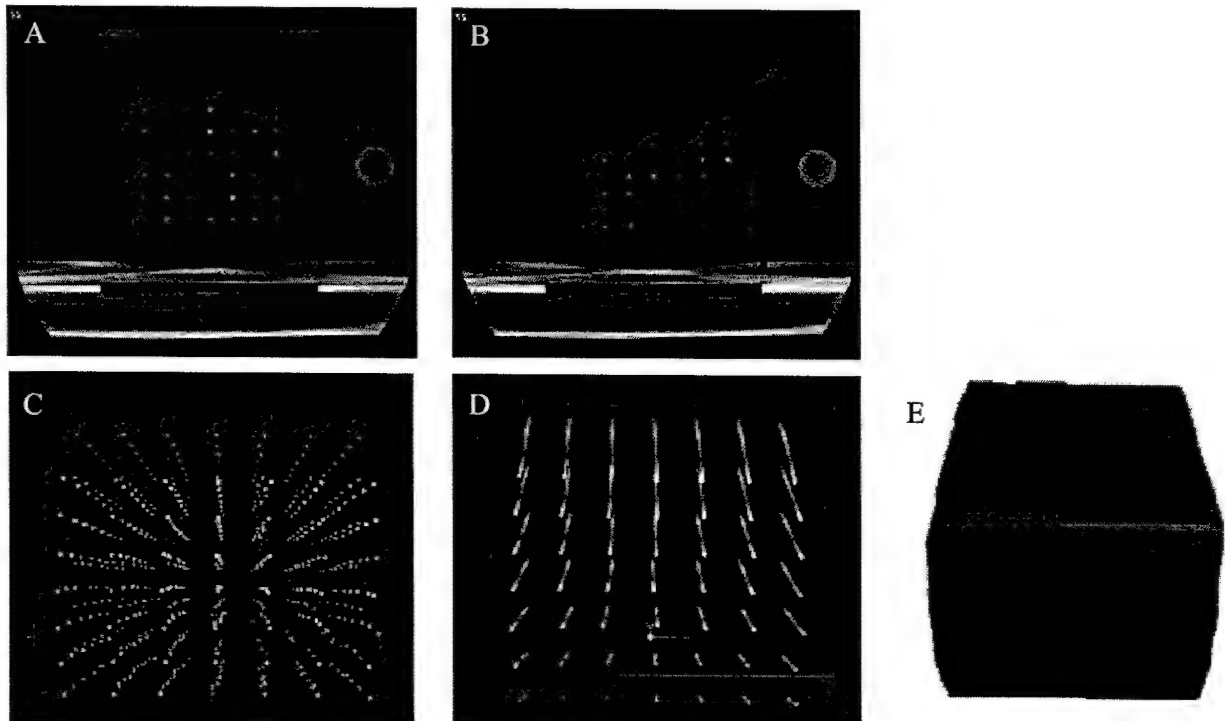


Figure 4: The CT image of the central x - z plane of the "Truth Cube" after segmentation in both the (A) unloaded and (B) maximally compressed states; the upper registration sphere is noticeable in these images. (C) 3_d perspective view of the centroids of best-fit spheres for all 343 beads in all strain states (blue = unloaded, green = 5%, red = 12.5 %, yellow = 18.25% strain). (D) Trajectory of the beads in the x - z central plane of (C). (E) Outer surfaces of the cube in its 4 strain states (purple = unloaded, red = 18.25%).

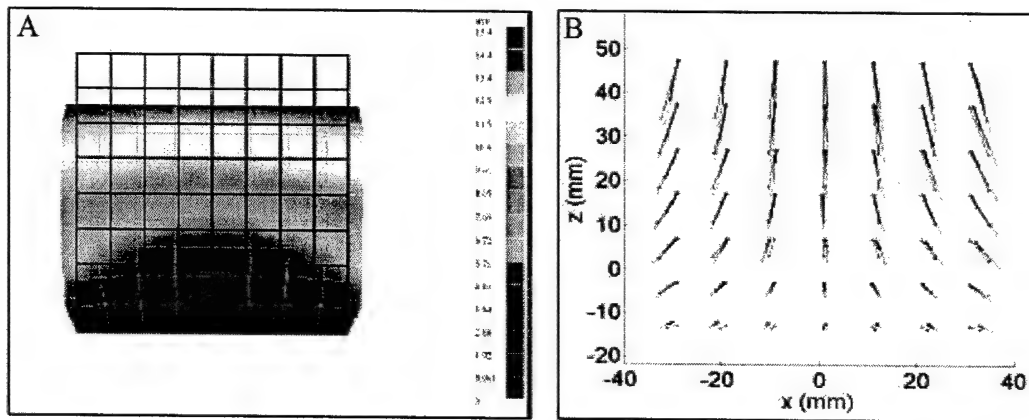


Figure 5: A comparison of the finite element displacement field and the CT experimental data displacement field for the central XZ plane. (A) A picture of the displacement of the uncompressed (black) and compressed (colored) mesh. (B) A comparison of the finite element results (thin black lines) and experimental results (grey-scale lines).

Bead initial location			Displacement (FEM)			Displacement (experimental)			Exp disp - FEM disp
X [mm]	Y [mm]	Z [mm]	dX [mm]	dY [mm]	dZ [mm]	dX [mm]	dY [mm]	dZ [mm]	
-29.0	3.0	-47.0	-3.3	0.0	12.9	-1.3	0.7	15.3	3.3
-19.0	3.0	-47.0	-2.3	0.0	12.7	0.0	0.7	15.2	3.5
-9.0	3.0	-47.0	-1.2	0.0	12.6	0.6	0.4	15.1	3.1
1.0	3.0	-47.0	0.0	0.0	12.6	1.3	0.4	15.1	2.8
11.0	3.0	-47.0	1.2	0.0	12.6	3.1	0.6	14.9	3.0
...
...
-9.0	3.0	13.0	-0.6	0.0	0.6	-0.6	0.4	1.2	0.7
1.0	3.0	13.0	0.0	0.0	0.7	0.1	0.2	1.1	0.4
11.0	3.0	13.0	0.6	0.0	0.6	0.7	0.2	1.3	0.7
21.0	3.0	13.0	1.3	0.0	0.8	1.8	0.1	1.2	0.6
31.0	3.0	13.0	2.1	0.0	0.6	3.0	0.0	1.8	1.5

Table 1: A representative set of 10 bead locations at rest and after 18.25% strain (14.6 mm compression) evaluated by both FEM and experimental data. The final column is the difference in bead location between the two evaluations.

These results are readily compared with the output of computational models. The simple FEM calculation presented here used a minimal number of elements to reflect some of the speed-vs-accuracy tradeoffs of real-time tissue simulations. The maximum differences with the experimental results were on the order of 3.5 mm for a displacement of about 15 mm. This is a relatively small difference, as might be expected for these simple geometric and loading conditions, and considering the estimated 2 mm accuracy of the measurement. Some portion of the difference may also be due to inexact specification of the boundary conditions on the top of the cube during compression. Nonetheless, refinement of the model (e.g. smaller mesh size) should bring closer agreement to the experiment. For more complex geometries, materials, and loading conditions, much larger differences can be expected between FEM results and reality, which this type of experimental data can help quantify.

Several refinements to the measurement techniques are indicated by these results. First, we have only estimated the accuracy of the bead positions in this initial dataset. More precise accuracy specifications can be obtained through an analysis of the imaging and image processing procedures, and through reproducibility measurements. The raw scan data will be available on the web site, so other users are also welcome to develop improved image processing algorithms for this purpose. Another area for better characterization is the top surface boundary condition, where oiling the cube served to limit and regularize friction, but where a "frictionless" condition clearly did not apply. Fortunately, the contact area is readily measured during the experiment and in the processed CT images, so additional boundary information is available.

4.1 Future Work

Our immediate plans are to complete tests of the truth cube, with a goal of improving the accuracy of the

fiducial position estimation process and the boundary conditions. We will also develop additional loading capabilities, including indentation, shear, and torsion, to better reflect the range of surgical manipulations.

While this initial study demonstrated the feasibility of experimental measurement of volumetric displacement fields for soft materials under large strains, the truth cube itself is of limited value for validating soft tissue models. The cube has regular geometry and material properties that are helpful for the development process, but fast tissue simulations must deal with conditions that are vastly different, involving very large deformations, irregular shapes and complex materials. These are also the conditions where validation using traditional FEM techniques is most problematic.

The next phase of this project is thus the measurement of biological tissue volumetric displacements, in the form of an entire organ. Preliminary plans call for measurement of a porcine liver immediately post mortem. Fiducials will be inserted via needles throughout the parenchyma, followed by the imaging and image processing procedures reported here. In addition, a cast of the external shape of the liver will enable the creation of a silicone rubber model with bead fiducials where the material properties will be well-characterized. Simulation developers can then separately consider issues of large deformation and material complexities.

While these biological material tests have obvious advantages, the material properties will not be well-characterized as in the rubber tests. The identification of these material properties is an active area of research, and the data sets may be useful for solving the inverse problem of estimating these material properties from the displacement data. In any case, the data will provide a source of information for the development of fast simulation systems.

As we proceed, we welcome comments and suggestions on all aspects of the project, from tissue selection and loading conditions to experimental methods and data analysis. Further information is provided on the web site at:

<http://biorobotics.harvard.edu/truthcube>. Contributions of a broad cross-section in the tissue modeling community will help ensure the development of a robust physical standard for the benchmarking of real-time soft tissue simulations.

4. Acknowledgements

This work was supported by U.S. Army Medical Research

Acquisition Activity under contract DAMD17-01-1-0677. The Whitaker Foundation provided graduate student support.

6. References

- [Ast98] Astley, O., Hayward, V. *Multirate haptic simulation achieved by coupling finite element meshes through norton Equivalents*. Proc. IEEE Int. Conf. on Robotics and Automation, 1998.
- [Cot96] S. Cotin, H. Delingette, J.M. Clément, M. Bro-Nielsen, N. Ayache, J. Marescaux: *Geometrical and Physical Representations for a Simulator of Hepatic Surgery*, Proc. Medicine Meets Virtual Reality IV (MMVR'96), 1996, pp. 139-150.
- [De01] S. De, J. Kim and M.A. Srinivasan. *Virtual surgery simulation using a collocation-based method of finite spheres*. First M.I.T. Conference on Computational Fluid and Solid Mechanics, 2001.
- [Kuh97] Kühnapfel UG, Kuhn C, Hübner M, Krumm HG, MaaE H, Neisius B. *The Karlsruhe Endoscopic Surgery Trainer as an example for virtual reality in medical education*, Minimally Invasive Therapy and Allied Technologies, 1997;(6):122-125.
- [Osm00] Osman, N.F.; McVeigh, E.R.; Prince, J.L. *Imaging heart motion using harmonic phase MRI*. IEEE Transactions on Medical Imaging vol.19, no.3 186-202 March 2000.
- [Ott01] M. Ottenmeyer, *Minimally Invasive Instrument for In Vivo Measurement of Solid Organ Mechanical Impedance*, Doctoral Thesis in Mechanical Engineering at the Massachusetts Institute of Technology. © M.I.T., 2001.
- [Pic01] G. Picinbono, H. Delingette, and N. Ayache. *Non-linear and anisotropic elastic soft tissue models for medical simulation*. In ICRA2001: IEEE International Conference Robotics and Automation, Seoul Korea, May 2001.
- [Pip91] Pipe, J.G.; Boes, J.L.; Chenevert, T.L. Method for measuring three-dimensional motion with tagged MR imaging *Radiology*181: 591, 1991.
- [Str98] N. Strumas, O. Antonyshyn, M.J. Yaffe, G. Mawdsley, and P. Cooper. *Computed Tomography Artifacts: an experimental investigation of causative factors*. Canadian Journal of Plastic Surgery, 1998; 6(1):23-29.
- [Wel00] P.W. Wellman, R.D. Howe. *Breast tissue stiffness in compression is correlated to histological diagnosis*. Submitted to the Journal of Biomechanics. 2000.
- [Wel99] P.W. Wellman. *Tactile imaging*. Ph.D. Thesis, Division of Engineering and Applied Sciences, Harvard University, 1999.
- [Zha97] M. Zhang, Y.P. Zheng, and A.F.T. Mak. *Estimating the effective Young's modulus of soft tissues from indentation tests - nonlinear finite element analysis of effects of friction and large deformation*. Med. Eng. Phys. Vol. 19, No. 6 pp512-517, 1997.

Appendix B: selected CVs and BioSketches

Dawson, Steven L., M.D.

Howe, Robert D., Ph.D.

Ottensmeyer, Mark P., Ph.D.

Kerdok, Amy E., M.S

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.
Photocopy this page or follow this format for each person.

NAME Steven L. Dawson, MD	POSITION TITLE Program Lead, Medical Simulation, CIMIT
----------------------------------	---

EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i>)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
State University of New York at Buffalo	BA	1974	Biology
Tufts University	MD	1978	Medicine
Medical-Surgical Intern, Newton-Wellesley Hospital		1978-1979	
Radiology Residency, Massachusetts General Hospital		1979-1982	
Imaging and Interventional Radiology Fellowship, Massachusetts General Hospital		1982-1984	

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. **DO NOT EXCEED TWO PAGES.**

Professional Experience:

1982-1986	Radiologist, Waltham Hospital
1986-1990	Radiologist, Lahey Clinic
1990-Present	Interventional Radiologist, Massachusetts General Hospital
1997-1999	Director, New Initiatives, Center for Innovative Minimally Invasive Therapy
1998-1999	Director, Education, Center for Innovative Minimally Invasive Therapy
1998-Present	Program Lead, Medical Simulation, CIMIT
1994-2001	Assistant Professor, Harvard Medical School
2001-	Associate Professor, Harvard Medical School

Honors:

1974	Phi Beta Kappa
1992	RSNA Exhibit: Lee MJ, Dawson SL, Mueller PR. Percutaneous management of periportal biliary malignancies with metallic endoprostheses: results, technical problems and causes of failure. Certificate of Merit Award.
1990	Associate Editor, <i>Seminars in Interventional Radiology</i>
1991	Reviewer, <i>American Journal of Roentgenology</i>
1994	Member, American College of Radiology Expert Panel on Interventional Radiology of ACR Task Force on Appropriateness Criteria
1994	Fellow, Society of Cardiovascular and Interventional Radiology
1996	Technology Reviewer, Image Guided Medicine, Technology Applications Review, National Technology Transfer Center
1997	Examiner, American Board of Radiology Subspecialty Examination in Vascular and Interventional Radiology
1995	Corresponding Fellow, Cardiovascular and Interventional Radiology Society of Europe
1996	External Reviewer, Biomedical Programs, Battelle/Pacific Northwest National Labs
1999	Session Chair and Lecturer, US Public Health Service and National Cancer Institute Joint Working Group on Image Guided Diagnosis and Treatment
2000	Partners Excellence Award

Research Interests:

Minimally invasive treatments of visceral cancer using image guidance, computer-based simulations for medical learning

Selected Publications:

Lee MJ, Mueller PR, Dawson SL, Gazelle GS, Hahn PF, Goldberg MA, Boland GW. Percutaneous Ethanol Injection for the Treatment of Hepatic Tumors: Indications, Mechanism of Action, Technique and Efficacy. *AJR* 1995; 164: 215-220.

Goldberg SN, Gazelle GS, Dawson SL, Rittman WJ, Mueller PR, Rosenthal DI. Tissue Ablation with Radiofrequency Using Multiprobe Arrays. *Academic Radiology* 1995; 2: 670-674.

Goldberg SN, Gazelle GS, Dawson SL, Rittman WJ, Mueller PR, Rosenthal DI. Tissue ablation with radiofrequency: effect of probe size, gauge, duration, and temperature on lesion volume. *Academic Radiology* 1995; 2:399-404.

Rattner DW, Dawson SL. The Operating Room of the Future, in Current Review of Laparoscopy, Churchill Livingstone, 1995, 185-193s.

Dawson SL, Rattner DW. "Minimally Invasive Therapies, Imaging and Energy Delivery Systems", in Strategies for the Future. The Role of Technology in Reducing Health Care Costs. Sandia National Laboratories, November, 1996, pp. 91-116.

Goldberg SN, Ryan TP, Hahn PF, Schima W, Dawson SL, Lawes KR, Mueller PR, Gazelle GS. Transluminal radiofrequency tissue ablation with use of metallic stents. *JVIR* 1997; 8: 835-843.

Dawson SL, Kaufman JA. The Imperative for Medical Simulation. *Proceedings of the IEEE* 1998; 86 (3): 479-483.

Cotin SC, Dawson SL, Meglan D, Shaffer DW, Ferrell MA, Sherman P, et al. ICTS, an interventional cardiology training system. *Medicine Meets Virtual Reality 2000*, IOS Publishing, (70):59-65.

Shaffer D, Meglan D, Ferrell M, and Dawson S. Virtual Rounds: simulation-based education in procedural medicine. In: Pien H, editor. *Battlefield Biomedical Technologies*, Proc. SPIE 1999; 3712:99-108.

Shaffer DW, Dawson SL, Meglan D, Ferrell M. Simulation Based Education in Procedural Medicine, Proc. SPIE Conference on Battlefield Biomedical Technologies, v.3712, April, 1999.

Bauer JJ, Magee JH, Moses G, Leitch R, Dawson SL. Medical simulation training initiative (MSTI), SPIE Conference on Battlefield Biomedical Technologies, v.4037, April, 2000.

Cotin SC, Dawson SL. CAML: a general framework for the development of medical simulation systems. SPIE Conference on Battlefield Biomedical Technologies, v.4037, April, 2000.

Dawson SL, Cotin S, Meglan D, Shaffer DW, Ferrell MA. Designing a computer-based simulator for interventional cardiology training [with editorial]. *Catheterization and Cardiovascular Interventions*, 2000; 51; 522-528.

Shaffer, DW, Dawson, SL, Meglan, D, Cotin, S, Ferrell, M, Norbash, A, Muller, J. (2000) "Design Principles for the use of simulation as an aid in interventional cardiology training." *Minimally Invasive Therapy and Applied Technologies*, 10:2.

NAME Robert D. Howe, Ph.D.		POSITION TITLE Gordon McKay Professor of Engineering	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include post-doctoral training.)			
INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
Reed College – Portland, OR	B.A.	1979	Physics
Stanford University – Stanford, CA	M.S.	1985	Mechanical Engineering
Stanford University – Stanford, CA	Ph.D.	1990	Mechanical Engineering

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds two pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Employment

1979-1981 Electronics Engineer, Kratos Display Systems. Los Gatos, CA.
1981-1983 Research Physicist, High Temperature Gasdynamics Laboratory, Stanford University
1984-1990 Research Assistant, Mechanical Engineering Dept. Stanford.
1990-1994 Assistant Professor of Mechanical Engineering, Harvard University.
1994-1997 Associate Professor of Mechanical Engineering, Harvard University.
1997-present Gordon McKay Professor of Engineering, Division of Engineering & Applied Sciences, Harvard Univ.

Selected Honors and Professional Service

National Science Foundation Young Investigator Award, 1993.
Best poster award, Sixth International Meeting of the Society for Minimally Invasive Therapy, Berlin (with William Peine), 1994.
Associate editor, IEEE Transactions on Robotics and Automation, 1994-1998.
Funding Review Panel Member, National Science Foundation, 1994, 2000.
Whitaker Foundation Biomedical Engineering Research Grant (Career Development Award), 1995.
Chair and Organizer, Annual Symposium on Haptic Interfaces for Virtual Environment and Teleoperator Systems, ASME International Mechanical Engineering Congress and Exposition, 1996-1998 (with Susan J. Lederman).
Program Committee, International Symposium on Medical Robotics and Computer Assisted Surgery/MICCAI, 1994, 1995, 1997, 1998, 2000.
Program Committee, Frontiers of Engineering Symposium, National Academy of Engineering, Irvine, CA, Nov. 1998.

Selected Publications

Wellman, P.S, Dalton, E.P., Krag, D., Kern, K.A., Howe, R.D. "Tactile Imaging of Breast Masses: First Clinical Report," Archives of Surgery, in press.
A. Z. Hajian and R. D. Howe, "Biomechanics of Manipulation: Grasping the Task at Hand," in J. Winters and P. Crago,

- eds, Neural Control of Posture and Movement, Springer-Verlag, 2000, pp.382-389.
- F. Lai and R.D. Howe, "Evaluating Control Modes for Constrained Robotic Surgery," Proc. IEEE International Conference on Robotics & Automation, San Francisco, April 2000, pp. 603-609.
- Pawluk, D.T.V. and Howe, R.D. "Dynamic contact of the human fingerpad against a flat surface." ASME Journal of Biomechanical Engineering 121(6):605-611, December 1999.
- M. Shibata and R.D. Howe, "Effect of Gloving on Perceptual and Manipulation Task Performance," in N. Olgac, ed., Proc. ASME Dynamic Systems and Control Division, 1999, DSC-Vol. 67.
- P. Dupont, T. Schulteis, P. Millman, and R. D. Howe, "Automatic Identification of Environment Haptic Properties," Presence 8(4):392-409, August 1999.
- Pawluk, D.T.V. and Howe, R.D. "Dynamic Lumped Element Response of the Human Fingerpad." ASME Journal of Biomechanical Engineering 121(2):178- 184, April 1999.
- R. D. Howe and Y. Matsuoka, "Robotics for surgery," Annual Review of Biomedical Engineering, 1:211-240, 1999.
- W.J. Peine and R.D. Howe, "Do humans sense finger deformation or distributed pressure to detect lumps in soft tissue?," in R.J. Furness, ed., Proc. of the ASME Dynamic Systems and Control Division, ASME International Mechanical Engineering Congress and Exposition, Anaheim, Nov. 19-20, 1998, DSC-Vol. 64, pp. 273-278.
- D. T. V. Pawluk, J. S. Son, P. S. Wellman, W. J. Peine, and R. D. Howe. "A Distributed Pressure Sensor for Biomechanical Measurements," ASME Journal of Biomechanical Engineering 102(2):302- 305, April 1998.
- A. Z. Hajian and R. D. Howe, "Identification of the mechanical impedance at the human finger tip," ASME Journal of Biomechanical Engineering, 119(1):109-114, Feb. 1997. Also presented at the International Mechanical Engineering Congress, American Society of Mechanical Engineers, Chicago, IL, November 1994, Proceedings ed. C. J. Radcliffe, DSC-vol. 55-1, p. 319-327.
- Pawluk D. and Howe, R.. A Holistic Model of Human Touch. In J.M. Bower (Ed.) Computational Neuroscience Trends in Research, Plenum Press, New York, pp. 759-764, 1997.
- P. E. Dupont, T. M. Schulteis, and R. D. Howe , "Experimental Identification of Kinematic Constraints, Proc. IEEE International Conference on Robotics and Automation, Albuquerque, New Mexico, April 20 - 25, 1997, pp. 2677-82.
- R. D. Howe, D. A. Kontarinis, W.J. Peine, and P. W. Wellman, "Tactile displays for increased spatial and temporal bandwidth in haptic feedback," in Y. Shirai and S. Hirose, eds., Robotics Research: The Eighth International Symposium, October 4-7, 1997, Hayama, Japan, Springer-Verlag, 1998.
- P. S. Wellman, R. D. Howe, N. Dewagan, M. A. Cundari, E. Dalton, K. A. Kern, "Tactile Imaging: A Method for Documenting Breast Masses," Proc. 1st Joint BMES/EMBS Conference, Atlanta, Oct. 13-16, 1999, p. 1131.
- D.T.V. Pawluk, R.D. Howe, "Dynamic Contact Mechanics of the Human Fingerpad with a Flat Surface," Biomedical Engineering Society Annual Meeting, Cleveland, October 11 , 1998.
- D. T. V. Pawluk and R. D. Howe, "Contact pressure distribution on the human finger pad," 26th Congress of the International Society of Biomechanics, Tokyo, August 25-29, 1997, p. 335.
- Pawluk, D.T.V., Peine, W.J., Wellman, P.S. and Howe, R.D., "Simulating Soft Tissue with a Tactile Shape Display," Advances in Bioengineering, ASME BED-Vol. 36, pp. 253-4.
- P. S. Wellman and R. D. Howe, "Modeling probe and tissue interaction for tumor feature extraction," 1997 ASME Summer Bioengineering Conference, Sun River, Oregon, June 1997, BED-Vol. 35, p. 237-8.
- D. T. V. Pawluk and R. D. Howe, "Mechanical impedance and energy dissipation in the human finger pad," 1997 ASME Summer Bioengineering Conference, Sun River, Oregon, June 1997, BED-Vol. 35, p. 591-592.
- W.J. Peine and R. D. Howe, "Finger pad shape in lump detection," 1997 ASME Summer Bioengineering Conference, Sun River, Oregon, June 1997, BED-Vol. 35, p. 593-594.
- R. D. Howe, W. J. Peine, D. A. Kontarinis, and J. S. Son, "Remote palpation technology," IEEE Engineering in Medicine and Biology, 14(3):318-323, May/June 1995.

NAME Mark P. Ottensmeyer, Ph.D.		POSITION TITLE Research Fellow, Simulation Group, CIMIT, MGH	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include post-doctoral training.)			
INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
McMaster University, Hamilton, Ontario, Canada	B.Eng.Mgt	1994	Mechanical Engineering and Management
Massachusetts Institute of Technology, Cambridge, MA, USA	M.S.M.E.	1996	Mechanical Engineering
	Ph.D.	2001	Mechanical Engineering

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds two pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Research Experience

1991-1993 (summers) Research Assistant, McMaster University, Canada. Performed wind-tunnel experiments on electrical transmission line models to study transmission line galloping phenomenon. PI: Prof. Ozden F. Turan.

1993-1994 (summers) Research Assistant, Flexible Manufacturing Systems Laboratory, McMaster University, Canada. Developed power-up calibration system for AdeptOne industrial robot. PI: Prof. Hoda ElMaraghy.

1994-1996 Research Assistant, Human-Machine Systems Laboratory, M.I.T. Conducted research into and designed experiments on human performance in teleoperated surgery exercises with system time delays. PI: Prof. Thomas B. Sheridan.

1996-1998 Research Assistant, Haptics Group, Artificial Intelligence Laboratory, M.I.T. Developed thermal feedback device for virtual environment touch interface. PI: Dr. J. Kenneth Salisbury

1998-2001 Research Assistant, Haptics Group, Artificial Intelligence Laboratory, M.I.T. Developing minimally invasive surgical instruments for measuring mechanical properties of living organ tissues, performing *in vitro* and *in vivo* measurements. PI: Dr. J. Kenneth Salisbury

2001-present Research Fellow, Simulation Group, Center for Integration of Medicine and Innovative Technology, Massachusetts General Hospital. Developing minimally invasive surgical instruments for measuring mechanical properties of living organ tissues, performing *in vitro* and *in vivo* measurements, designing simulator for surgical training. P.I. Dr. Steven Dawson

Honors

1989 Ontario Scholarship
Sir Isaac Newton Physics Contest, Book award
1990 S.L. Squire Scholarship, McMaster University
Harry Lyman Hooker Scholarship, McMaster University
1991 Whidden Hall Residence Scholarship, McMaster University
Harry Lyman Hooker Scholarship, McMaster University

- 1992 Shell Canada Series Scholarship, McMaster University
 Ray Lawson Scholarship, McMaster University
- 1993 Shell Canada Series Scholarship in Engineering and Management, McMaster University
 Ray Lawson Scholarship, McMaster University
- 1996-1998 Post Graduate Scholarship, National Sciences and Engineering Research Council, Canada

Society Memberships

Sigma Xi, The Scientific Research Society, Full Student Member, 5 years

ASME, Associate Member, 4 years

Publications

Refereed journal papers:

Ottensmeyer, Mark P., Hu, Jianjue, Thompson, James M., Ren, Jie, Sheridan, Thomas B. Investigations into performance of minimally invasive telesurgery with feedback time delays, *Presence: Teleoperators and Virtual Environments*, vol. 9, no.4, 369-82, 2000.

Ottensmeyer, Mark P. TeMPeST 1-D: an instrument for measuring solid organ soft tissue properties. *Experimental Techniques*, vol. 26, no. 3, 28-50, May/June 2002.

Conference papers:

Ottensmeyer, Mark P., Salisbury, J. Kenneth. Hot and Cold Running VR: adding thermal stimuli to the haptic experience. Proceedings of the Second PHANTOM User's Group Workshop, AI Lab Technical Report 1617, Endicott House, Dedham, MA. pp34-37. 19-22 Oct 1997.

Thompson, J.M., Ottensmeyer, M.P., Sheridan, T.B. Human Factors in Tele-inspection and Tele-surgery: Cooperative Manipulation under Asynchronous Video and Control Feedback. Proceedings of the Medical Image Computing and Computer-Assisted Intervention 1st International Conference, MICCAI '98, Cambridge, MA. pp368-377. 11-13 Oct 1998.

Ottensmeyer, Mark P., Ben-Ur, Ela, Salisbury, Dr. J. Kenneth. Input and Output for Surgical Simulation: Devices to Measure Tissue Properties *in vivo* and a Haptic Interface for Laparoscopy Simulators. Proceedings of Medicine Meets Virtual Reality 2000, Newport Beach, CA. IOS Press. pp236-242. 27-30 Jan 2000.

Ottensmeyer, M.P., Salisbury, J.K. *In vivo* mechanical tissue property measurement for improved simulations. Proceedings of Digitization of the Battlespace V and Battlefield Biomedical Technologies II, R. Suresh and H.H. Pien, Eds., Proc. SPIE 4037, Orlando, FL. in press. 24-28 Apr 2000.

Bruyns, Cynthia, Ottensmeyer, Mark. Measurements of Soft-Tissue Mechanical Properties to Support Development of a Physically Based Virtual Animal Model. *MICCAI 2002. Proceedings of the Medical Image Computing and Computer-Assisted Intervention 5th International Conference*, Tokyo, Japan, accepted for publication. 25-28 Sept 2002.

Cotin, Stephane, Stylopoulos, Nicholas, Ottensmeyer, Mark, Neumann, Paul, Rattner, David, Dawson, Steven. Metrics for Laparoscopic Skills Trainers: The Weakest Link!. *MICCAI 2002. Proceedings of the Medical Image Computing and Computer-Assisted Intervention 5th International Conference*, Tokyo, Japan, accepted for publication. 25-28 Sept 2002.

Other publications:

Ottensmeyer, Mark Peter. Telerobotic Surgery: Feedback Time Delay Effects on Task Assignment. Master's Thesis in Mechanical Engineering at the Massachusetts Institute of Technology. © M.I.T., 1996.

Ottensmeyer, Mark Peter. Minimally Invasive Instrument for In Vivo Measurement of Solid Organ Mechanical Impedance. Doctoral Thesis in Mechanical Engineering at the Massachusetts Institute of Technology, © M.I.T., 2001.

AMY ELIZABETH KERDOK

Home:
2443 Massachusetts Ave #12
Cambridge, MA 02140
Tel: (617) 945-0929
Email: kerdok@fas.harvard.edu

Work:
29 Oxford St.
Harvard University Pierce Hall B-11B
Tel: (617) 496-9098
Fax: (617) 495-9837

EDUCATION

HARVARD UNIVERSITY

- Candidate for Ph.D. in Engineering Sciences, Division of Engineering and Applied Sciences
- Harvard/MIT Division of Health Sciences and Technology Medical Engineering/Medical Physics student

Cambridge, MA
expected 2004

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

- MS, Mechanical Engineering
- GPA: 4.8 / 5.0

Cambridge, MA
September 1999

RENSSELAER POLYTECHNIC INSTITUTE

- BS, Biomedical Engineering;
- Concentration: Mechanical engineering
- Minor: Management
- GPA: 3.97 / 4.0 (*summa cum laude*)

Troy, NY
May 1997

ACADEMIC EXPERIENCE

HARVARD UNIVERSITY

Research Assistant

- Area: Soft tissue characterization for robotic surgery and simulation
- Advisor: Prof. Robert Howe, Biorobotics Laboratory
- Responsibilities: Mechanical design of soft tissue material property testing device, clinical data collection, constitutive law modeling, validation

Cambridge, MA
2000 – present

HARVARD UNIVERSITY

Teaching Fellow

- Taught and assisted in developing ES51 "Computer Aided Design"
- Assisted in teaching and grading ES149 "Muscles, Reflexes, and Locomotion"

Cambridge, MA

Spring 2002

Spring 2001

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Research Assistant

- Area: Sports Biomechanics
- Advisors: Prof. Thomas A. McMahon, Harvard University Division of Engineering and Applied Sciences, and Dr. Hugh M. Herr, MIT Leg Laboratory
- Responsibilities: Experimental apparatus design, human experimentation, computer simulation, physiologic testing, and modeling of the dynamic parameters of running.

Cambridge, MA
1998-2000

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Product Design and Development team project

- Designed and manufactured an alpha prototype of an energy returning forearm crutch

Cambridge, MA
Spring 1998

PROFESSIONAL EXPERIENCE

MEDSOURCE INC (formerly ACT MEDICAL INC.)

Project Engineer (graduate student intern)

- Involved in 3 projects: project manager for 1, co-managed other 2
- Responsibilities: proposal writing, customer relations, design and development of various medical products (from concept to prototyping to testing to manufacturing)

Newton, MA
January-August 2000

STRYKER (formerly HOWMEDICA INC.)

Research Technician, R&D, Performance Engineering

- Operated MTS 810 and 407 controller single axis dynamic testing machines
- Designed orthopedic testing fixtures and molds (under ISO, ASTM, and FDA standards)

Rutherford, NJ
Summer 1995

HARVARD MEDICAL SCHOOL, New England Regional Primate Center
Intern, dept. of Cardiovascular Medicine with Dr. Stephen Vatner

Southboro, MA
Summer 1994

- Assisted as the third person in open heart animal surgeries
- Assisted Dr. Luc Hittenger in experiment on Left Ventricular Hypertrophy Dogs

PATENTS AND PUBLICATIONS

Kerdok, A. E., S. M. Cotin, M. P. Ottensmeyer, A. M. Galea, R. D. Howe, and S. L. Dawson. Truth Cube: Establishing Physical Standards for Real Time Soft Tissue Simulation. *Medical Image Analysis*, submitted August 2002.

Walczyk D. F., and Kerdok A. E. Mechanical Weight Bearing Indicator for the Foot: Rensselaer Polytechnic Institute. U.S. Patent No. 6,405,606 B1, June 18, 2002.

Kerdok, A. E., A. A. Biewener, T. A. McMahon, P. G. Weyand, and H. M. Herr. Energetics and Mechanics of Human Running on Surfaces of Different Stiffnesses. *Journal of Applied Physiology* 92: 469-478, 2002.

Kerdok, A. E. Energetics and Mechanics of Human Running on Surfaces of different Stiffnesses. MS, Mechanical Engineering, Massachusetts Institute of Technology Cambridge, 1999.

LEADERSHIP EXPERIENCE

RENSSELAER POLYTECHNIC INSTITUTE

Troy, NY

- Student Representative for the Archer Center for Student Leadership
Organized Anderson Consulting Leadership conference 1996
- Engineering Leadership course Spring 1996
- Professional Leadership Program, selected group of juniors 1995-1996
Developed skills for team and leadership aspects of the professional world
- Pi Beta Phi executive board elected positions 1995-1996
Housing Committee Representative, Membership Chairman
- Team Leader, Introduction to Engineering Design team, Fall 1994
Delegated duties to design a pipe inspection robot to plot grade vs. distance

AWARDS & HONORS

Whitaker Fellowship, for advanced studies in Biomedical Engineering 1997-2002
Sigma Xi (national research honor society) inducted 1998
Livingston W. Houston Citizenship Award, RENSSELAER POLYTECHNIC INSTITUTE 1997
Paul B. Diach Award, top biomedical student, RENSSELAER POLYTECHNIC INSTITUTE 1997
Olympia, athletic honor society, RENSSELAER POLYTECHNIC INSTITUTE 1997
Panhellenic Top Scholar, RENSSELAER POLYTECHNIC INSTITUTE 1997
Founder's Award for Excellence, RENSSELAER POLYTECHNIC INSTITUTE 1995
White Key Society, Jr. honor society, RENSSELAER POLYTECHNIC INSTITUTE 1994-1997
Tau Beta Pi (national engineering honor society) inducted 1996
Rensselaer Alumni Scholarship 1993
RENSSELAER POLYTECHNIC INSTITUTE medal (mathematics and science scholarship) 1992

ATHLETICS

Harvard University Cycling Association, road team, Nationals 2002
Boston-to-New York AIDS Ride 5 1999

- 3-day 275 mile bike ride, personally raised over \$2500

RENSSELAER POLYTECHNIC INSTITUTE

- Varsity Soccer, Most dedicated, UCAA All-Academic team, Captain 1993-1996
- Varsity Basketball 1993-1994
- Varsity Lacrosse 1995-1996